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ETAMON AND MUSCLE SPASM

ITS CLINICAL APPLICATION

N. L. WULFSOHN, M.B., B.CH. (RAND)
Grey's Hospital, Pietermaritzburg

Skeletal muscle spasm has proved to be an incapacitating symptom for which adequate relief is still not yet at hand. In 1949 Lannon and Braudo [21] used Etamon (tetraethylammonium chloride) in the treatment of the muscle spasm of acute anterior poliomyelitis. The beneficial results obtained suggested the application of this drug to other types of spastic cases.

Perusal of the literature [23] has revealed no evidence of this wider application of Etamon and the good effects obtained in this short series seemed to warrant publication of the results.

Etamon has been used [3] so far for hypertension,[22] peripheral vascular disease,[1, 16] coronary artery disease, causalgia and in post-herpes zoster neuralgia, dysmenorrhoea, migraine headaches, multiple sclerosis [24] and in the muscle spasm of anterior poliomyelitis.[21]

However, there is no evidence, except for Lannon's work, that tetra-ethylammonium ions have been used for muscle spasm. The treatments so far for muscle spasm are many and varied. They include [8] sedative drugs such as phenobarbital and alcohol; anti-epileptic drugs such as Dilantin and Tridione; drugs of the nightshade family, such as Scopolamine and Stramonium; muscle-relaxing drugs such as Curare,[10, 14, 15, 18] Mephenesin,[18] Neostigmine,[8] procaine,[18, 19] procaine plus tribromethanol; [18] physiotherapy; [9, 25] local heat; [9, 15] and sympathectomy.[20] It is interesting to note that Royle,[20] in 1924, used sympathetic ganglionectomy with some beneficial effects in the treatment of spastic paralysis.

The first 17 consecutive cases which presented skeletal muscle spasm of whatever origin were treated with injections of Etamon. With three exceptions intravenous injections were given, the intramuscular route seeming to have, in comparison, very little effect.

The dosage used was 7 mg. per Kg. body weight given intravenously. Although not tried out, it has been suggested that the dosage be increased where necessary. Continuous intravenous drip has also been suggested.

In this series of cases toxic effects [4] were observed in three cases. They were irregular respiration, intestinal colic and an irregular pulse. The latter two effects were transitory. Guyton and Reeder [15] in a series of 400 cases, giving Etamon at least 1,000 times, noted very few serious effects and Lasser [3] *et al* found that toxic effects were infrequent. However, Björkenheim [5] says that old age, angina pectoris and peripheral sclerosis are absolute contra-indications to the use of the drug.

CASE REPORTS

These are summarized in Table I.

COMMENTS

It is interesting to note that in Case 14 Prostigmine, a parasympathomimetic drug, aggravated the patient's spastic condition where Etamon subsequently relieved it. Also, in Case 15, where Prostigmine was given to combat a side effect occurring after Etamon was given, the relaxed muscles almost immediately changed back to their former spastic state.

Following an intravenous injection the patient experienced a metallic sensation in the tongue, then a warm feeling in the legs and then the arms. He felt giddy, went pale and had a slurring speech which passed off in about 10 minutes. After 20-30 minutes the muscle tremor was reduced and the spasm was relieved to some extent. If the limb was now exercised a few times passively, an even more marked relaxation was apparent. Voluntary muscle control, however, was retained while the spasticity was relieved. In the lower limb the first few degrees of flexion from full extension gave the most resistance to active and passive movement.

The beneficial effects from one dose are only temporary, but in two cases with repeated injections a gradual improvement was apparent.

Physiotherapy (not used in these cases) is obviously indicated during the relaxed state of the muscle if the best results are to be obtained. Daily physiotherapy seems desirable.

With more numerous injections the muscle-relaxing effect, although still present, seemed to be less noticeable and more rapid.

There was little retrogression to the original state in two cases followed up three weeks after the cessation of a three weeks' course of intravenous injections.

TABLE I

No.	*Age*	*Sex*	*Race*	*Diagnosis*	*Duration of Muscle Spasm*	*No. of Injections*	*Effects*	*Remarks*
1.	35	Male	Bantu	Spastic hemiplegia due to cerebral thrombosis	9 months	1 (intravenous) injection	Marked improvement in active and passive movements. Effect lasted about 1 hour	
2.	55	Male	Non-European	Spastic hemiplegia following cerebral haemorrhage	1 month	1 (intravenous)	Spasticity relieved completely. Effect lasted about one hour	
3.	70	Female	European	Right spastic hemiplegia following cerebral haemorrhage	3 months	1 (intravenous)	Spasticity relieved completely and passive movements greatly increased in range. Effect lasted about one hour	Irregular pulse developed. Adrenalin given to counteract it
4.	20	Male	Non-European	Cerebral thrombosis and right spastic hemiplegia following rheumatic carditis with subacute bacterial endocarditis	3 months	1 (intravenous)	Marked increase in range and ease of movement. Could bend leg of his own accord which he said he could not do before	
5.	2	Male	European	Influenzal meningitis with right spastic hemiplegia	3 weeks	Intramuscular injections *b.d.* for one week	Spasticity relieved to some extent while injections were given	
6.	4	Male	Non-European	Tuberculous meningitis with right spastic hemiplegia	3 weeks	1 (intravenous)	Decreased sweating; irregular rapid respirations reduced to a more normal regular rate; spasm relieved almost completely and passive movements accomplished with ease which were not possible before. Effect lasted ± 2 hours	
7.	6	Female	Non-European	Tuberculous meningitis with right spastic hemiplegia	2 months	1 (intravenous)	Complete relief of spasm of right arm and some relief of the spasm of the back muscles and the right leg. Effect lasted ± 45 minutes	
8.	10 days	Male	Non-European	Tetanus neonatorum	10 days	1 (intravenous)	Tetanic convulsions resulting from stimulation were relieved completely	Irregular respiration followed injection. Adrenalin given later had no effect on the respiration
9.	6 days	Male	Non-European	Tetanus neonatorum	6 days	1 (intramuscular)	Relieved to some extent tetanic convulsions resulting from stimulation. Effect temporary	
10.	11	Female	European	Tension rigidity and athetosis	Since birth	1 (intravenous)	No effect on the rigidity. Intention tremor was temporarily reduced a little	
11.	23	Male	European	Quadriplegia plus athetosis (Little's disease)	Since birth	1 (intravenous) followed by 1 gm. *t.d.s.* intramuscular injections for 1 week	Almost complete relief of spasm of mouth, arms and legs; athetoid movements greatly diminished after the intravenous injection. Effect lasted about 2 hours	At the end of 1 week of intramuscular injections the patient was in the same condition as originally

TABLE I (*continued*)

No.	*Age*	*Sex*	*Race*	*Diagnosis*	*Duration of Muscle Spasm*	*No. of Injections*	*Effects*	*Remarks*
12.	55	Male	Non-European	Chronic parkinsonism. Tremor lower jaw and spastic quadriplegia	4 years	1 (intravenous)	Lower jaw tremor reduced to some extent. Increase of range and facility of active and passive movements of left arm and right leg	Right arm and left leg immobile due to fibrosis
13.	7	Female	Non-European	Spastic hemiplegia with epilepsy	4 months	2 (intravenous)	Marked increase of passive movement of arm and leg. Effect lasted ± 1 hour after each injection	
14.	6	Male	Non-European	Spastic quadriplegia with microcephaly	4 months	1 (intravenous); then every alternate day intramuscular injections for two weeks	Attacks of severe spasm aggravating basic condition were relieved. Active and passive movements of arms and legs markedly improved. Effect still present three weeks later	
15.	55	Male	European	?Amyotrophic lateral sclerosis with spastic right and left legs and right arm	Right leg 18 months; right arm and left leg 4 months	Intravenous injections every alternate day for 3 weeks	Complete relief of spasm of both legs and arm for about 1½ hours after first injection	Three weeks after cessation of injections: the number of attacks of spasm aggravating basic condition was reduced from 10–12 times in 12 hours to once or twice. Patellar and ankle clonus disappeared completely. Spasm of right arm was almost completely relieved. Spasm of left leg relieved less and of right leg still less. Patient could walk with far greater ease when helped and could stand alone, which he could not do before
16.	25	Male	Non-European	Hemisection of the spinal cord (stab wound); spastic paraplegia	1 month	1 (intravenous)	Spasm relieved almost completely. Intention tremor and clonus greatly reduced, active movement of limbs present, which were absent before; he could walk with far greater ease. This he observed himself. Effect lasted about 45 minutes.	
17.	17	Male	Non-European	?Tumour of medulla with right spastic hemiplegia	5 years	Intravenous injection given *b.d.* for 3 days then once a day for 3 days	One injection practically abolished tremor; capable of more movement in right leg. Spasticity in arm decreased to some extent	Effect one week after cessation of injections: spasticity about the same as originally, but movements of right leg were freer and the tremor was gone

The improvements were subjective and objective. The patient's appetite was improved and he slept better because the number of attacks of severe repeated spasms was reduced. The freer use of his limbs, which he felt was present, gave him more self-confidence and his outlook on the generally poor prognosis put to him was brightened. Psychologically he became much happier.

The muscle spasm was relieved and he was free to carry out voluntary movements, e.g., he could walk with far greater ease. The pain was relieved. Oedema of the limbs was reduced. The coldness of the limbs disappeared. Sweating was decreased. Ankle and patellar clonus was reduced and, in Case 15, disappeared completely.

DISCUSSION

The results in this short series indicate that Etamon might yet prove useful in the treatment of muscle spasm of various origins. They also favour Lannon and Braudo's suggestion[21] that spasm is due to sympathetic overactivity, resulting in heightened muscle tone, i.e., the clinical phenomenon known as spasm. Etamon,[12] it must be remembered, is a drug which blocks preganglionic impulses at the synapse of the sympathetic ganglia,[2, 6, 7, 11, 13] producing a depressor effect here,[17] a so-called 'paralyzing nicotinic action.'[16, 17]

Hence, once the spasm has been relieved, the voluntary movements are free and the muscles can then be re-educated along normal lines.

To obtain permanent results the primary disease causing the spasm must be dealt with. Etamon, or some other drug with a similar action, can only act symptomatically. The improvements obtained, however, seem to warrant its use in these conditions.

SUMMARY

1. Seventeen cases of skeletal muscle spasm have benefited from the use of Etamon.

2. Intravenous had a more marked effect than intramuscular injections.

3. The results showed a temporary relief from muscle spasm and tremor.

4. When repeated injections were given the result was more lasting.

5. Physiotherapy should be used as an important adjuvant.

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NEW PREPARATIONS AND APPLIANCES

CHEMICAL TREATMENT OF HYPERTENSIVE CONDITIONS

Pentamethonium bromide is a member of the alkamethonium group of compounds, one of which was recently reported on under the heading *Peptic Ulceration.* Pentamethonium bromide is related both chemically and in pharmacology to hexamethonium bromide, and also produces its effects by paralyzing transmission through autonomic ganglia. It is active when administered parenterally and orally, though results are more consistent with the intramuscular route.

The M & B Organization has made this drug available as Lytensium brand of pentamethonium bromide in presentations especially intended for the treatment of hypertensive conditions and peripheral vascular disorders, particularly Buerger's disease, Raynaud's syndrome, acrocyanosis, erythrocyanosis, hyperhidrosis and causalgia. These presentations are suitable for injection and for oral maintenance treatment.

In hypertension pentamethonium bromide would seem to be of value in investigating and selecting cases for sympathectomy, or in those cases where the results from sympathectomy have been disappointing or only of temporary benefit.

Treatment is normally initiated by intramuscular administration, which is well tolerated. A suitable adult dose is 50 to 100 mg. every 6-8 hours. The first doses should be given with the patient recumbent, until it is known to what degree posture will affect the fall in blood pressure. As individual response to the initial dosage is observed, the dose can be increased up to 150 mg. at an injection and may be maintained at this level, if tolerated, over a period of days. In the absence of contra-indications, ambulant treatment can be instituted.

Oral treatment produces a more delayed response, but of longer duration. The usual oral dose is approximately five times that of the intramuscular one, and may vary between 500 mg. three or four times daily to a total daily dosage of 4 gm.

Oral treatment is less consistent in results and the effects of intramuscular administration should therefore be fully observed before the change is made.

After a period of oral treatment blood pressures may rise again, necessitating a return to the intramuscular route for a time.

Very small initial stocks of the first two presentations shown below have already been received in Port Elizabeth, and the 40-oz. bottles should soon be available.

Lytensium brand Pentamethonium Bromide:—

10% solution—for intramuscular injection.

Boxes of 10 × 1 c.c. ampoules (each ampoule contains 100 mg. pentamethonium bromide).

Syrup—for oral administration. In bottles of 4 fluid ounces and bottles of 40 fluid ounces. (Each fluid drachm (3.6 c.c.) contains 500 mg. pentamethonium bromide.)

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EDITORIAL

STEROID THERAPY IN RHEUMATOID ARTHRITIS

Since the report by Hench, Kendall, Slocumb and Polley in 1949 [1] of the dramatic effects of Cortisone and ACTH (adrenocorticotrophic hormone) in rheumatoid arthritis, there has naturally been intense and widespread interest in the problems of steroid therapy of the 'rheumatic diseases'. Among these problems were two questions of outstanding importance:

1. Would these agents prove to be of real value in the actual treatment of cases of rheumatoid arthritis, and what was the mechanism whereby they exerted their beneficial effects?

2. Would other more readily available and cheaper steroids be effective in inducing remissions? Cortisone and ACTH were scarce and expensive and had undesirable 'side-effects'.

The answer to the first question is still not quite clear. There is a definite tendency for the disease to relapse, sooner or later, even after prolonged courses of therapy with Cortisone or ACTH. Hench *et al.*[2] have recently summarized their results on the effect of treating 23 cases of rheumatoid arthritis. The duration of therapy was as long as seven months in certain instances. After treatment was discontinued, eight patients maintained 60 to 90% of the improvement for seven to 14 months; five patients maintained about 50% of the improvement, and the other 10 patients maintained little or none of the improvement. Sprague [3] has summarized the present position by stating that the 'diseases which are favourably influenced by Cortisone and ACTH are not cured by them'.

The so-called 'side-effects' produced by these agents constitute another problem, although it does appear that the Cushing-like features produced are only temporary and subside when the medication is discontinued. However, it is well known that certain mental effects have been reported.[4] Rome and Braceland [5] have outlined the various mental changes which may occur. These vary from mild euphoria or depression to a hypomanic state or severer depression. In rare instances, psychoses have occurred, and it has been suggested that this is largely determined by the presence

1. Hench, P. S., Kendall, E. C., Slocumb, C. H. and Polley, H. F. (1949): Proc. Staff Meet. Mayo Clin., **24,** 181.
2. Slocumb, C. H., Polley, H. F., Hench, P. S. and Kendall, E. C. (1950): Proc. Staff Meet. Mayo Clin., **25,** 476.
3. Sprague, R. G. (1950): Proc. Staff Meet. Mayo Clin., **25,** 500.
4. Carlisle, J. M. (1950): Brit. Med. J., **2,** 590.
5. Rome, H. P. and Braceland, F. J. (1950): Proc. Staff Meet. Mayo Clin., **25,** 495.

VAN DIE REDAKSIE

STEROÏEDBEHANDELING VAN MISVORMENDE GEWRIGSONTSTEKING

Sedert Hench, Kendall, Slocumb en Polley in 1949 van die dramatiese uitwerking van Kortisone en ACTH (adrenokortikotrofiese hormoon) op misvormende gewrigsontsteking verslag gedoen het,[1] was daar natuurlik lewendige en wye belangstelling in die probleme van steroïedbehandeling van die 'rumatiese siektes'. Onder hierdie probleme was twee vraagstukke wat van besondere belang was:

1. Sal hierdie middels waarlik van belang blyk by die eientlike behandeling van gevalle van misvormende gewrigsontsteking en deur watter meganisme word hierdie heilsame gevolge te weeg gebring?

2. Sal ander steroïedes wat makliker beskikbaar en goedkoper is doeltreffend wees vir die verkryging van verligting? Kortisone en ACTH is skaars en duur en het ongewenste 'bykomende uitwerkinge'.

Die antwoord op die eerste vraag is nog nie heeltemal duidelik nie. Daar is 'n besliste neiging by die siekte om op een of ander tyd te hervat, selfs na langdurige tydperke van behandeling met Kortisone of ACTH. Hench *et al.*[2] het onlangs hulle uitslae van die behandeling se uitwerking op 23 gevalle van misvormende gewrigsontsteking opgesom. Die duur van die behandeling was in sommige gevalle selfs sewe maande lank. Nadat behandeling gestaak is, het agt pasiënte 60 tot 90% van die verbetering vir sewe tot 14 maande gehandhaaf, vyf pasiënte het ongeveer 50% van die verbetering gehandhaaf en die ander 10 pasiënte het met min of geen verbetering volgehou nie. Sprague[3] het die huidige toestand opgesom deur te verklaar dat 'die siektes waarop Kortisone en ACTH 'n gunstige uitwerking het nie deur hulle genees word nie'.

Die sogenaamde 'bykomende uitwerkinge' wat deur hierdie middels veroorsaak word, skep 'n ander probleem alhoewel dit wil voorkom of die Cushing-agtige kenmerke wat veroorsaak word, slegs tydelik is en afneem wanneer medisyne nie meer toegedien word nie. Dit is egter welbekend dat daar sekere uitwerkinge op die verstand aangemeld is.[4] Rome en Braceland[5] het die verskillende geestesverandering wat kan voorkom aangestip. Hulle wissel van 'n ligte welsynsgevoel of neerslagtigheid tot hipomaniese toestand of ernstiger bedruktheid. In buitengewone gevalle het psigoses voorgekom en daar word gemeen dat dié hoofsaaklik van die aanwesigheid van 'n abnormale voor-psigotiese persoonlikheid afhang. Hench meen dat die bykomende uitwerkinge eienskappe is waarmee geneeshere rekening

1. Hench, P. S., Kendall, E. C., Slocumb, C. H. en Polley, H. F. (1949): Proc. Staff Meet. Mayo Clin., **24,** 181.
2. Slocumb, C. H., Polley, H. F., Hench, P. S. en Kendall, E. C. (1950): Proc. Staff Meet. Mayo Clin., **25,** 476.
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4. Carlisle, J. M. (1950): Brit. Med. J., **2,** 590.
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of an abnormal pre-psychotic personality. Hench considers that the side-effects are features for which physicians must show respect, but not fear.

Thus, while Cortisone and ACTH are undoubtedly effective in inducing remissions in rheumatoid arthritis, the therapy requires careful attention and control, has undesirable side-effects, and tends to be followed by relapses to varying degrees after variable periods. Much still must be learnt about these drugs, about their mode of action, about the optimal method of administration, and about the prevention or control of undesirable side-effects. Until these data become available, the two agents should be employed as they are being used at the Mayo Clinic, not as established methods of therapy, but as useful tools for clinical investigation of a group of diseases hitherto peculiarly resistant to treatment.[6] It remains to be seen whether it will be possible to dissociate the beneficial therapeutic effect from the other physiological effects by means of interrupted courses of treatment, or by other methods. Cortisone is also effective orally in inducing remissions in rheumatoid arthritis and interesting data will be available on its role in therapy.

Hench[6] and Carlisle[4] agree that, despite many investigations, the fundamental nature of the action of Cortisone on disease processes is unknown. The opinion is commonly expressed that they exert their beneficial effects by affecting the reaction of tissues to various 'irritants'.

The sensational discovery made by Hench and Kendall led to attempts by other investigators to produce beneficial effects in rheumatoid arthritis by the use of other steroids, e.g. desoxycortone (desoxycorticosterone), progesterone, testosterone, pregnenolone, acetoxy-pregnenolone, etc. Conflicting results rapidly accumulated in the literature.

Lewin and Wassen[7] claimed that the simultaneous administration of desoxycortone and ascorbic acid caused a striking, rapid improvement in rheumatoid arthritis. They were strongly supported by le Vay and Loxton[8, 9] and by other observers in various parts of the world. However, the 12 medical members of the Empire Rheumatism Council of Great Britain expressed the decided view that this form of therapy was of no value in rheumatoid arthritis. The large majority of physicians familiar with rheumatoid arthritis, and with the effects of Cortisone and ACTH, were unimpressed by the claims made for desoxycortone and ascorbic acid; or by claims made for any of the agents listed above. A film was actually shown to the Press in London dealing with some of the cases of rheumatoid arthritis treated with desoxycortone and ascorbic acid, with le Vay and Loxton as medical advisers; but the wisdom of releasing the film was seriously questioned

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moet hou maar wat nie deur hulle gevrees moet word nie.

Alhoewel Kortisone en ACTH dus ongetwyfeld doeltreffend is vir die verkryging van verligting van misvormende gewrigsontsteking, vereis die behandeling noukeurige aandag en beheer, het dit ongewenste bykomende uitwerkinge en is dit na wisselende tydperke geneig om in verskillende grade te hervat. Veel meer kennis in verband met die geneesmiddels, hulle wyse van inwerking, die beste metode van toediening en die voorkoming of beheer van ongewenste bykomende uitwerkinge moet nog opgedoen word. Totdat hierdie gegewens beskikbaar word, moet die twee middels gebruik word soos by die Mayo-kliniek, nie as erkende behandelingsmetodes nie maar as nuttige middels vir die kliniese ondersoek van 'n groep siektes wat tot dusver besondere weerstand teen behandeling gebied het.[6] Daar moet nog gesien word of dit moontlik sal wees om deur middel van onderbroke behandelingsreekse of deur ander metodes die heilsame genesende uitwerking van die ander fisiologiese uitwerkinge te skei. Kortisone, wanneer dit deur die mond ingeneem word, is ook doeltreffend om verligting van misvormende gewrigsontsteking te verkry en belangwekkende gegewens oor die rol daarvan by behandeling sal beskikbaar wees.

Hench[6] en Carlisle[4] stem saam dat, ten spyte van baie ondersoeke, die fundamentele aard van die inwerking van Kortisone op siekteprosesse onbekend is. Die mening word gewoonlik uitgespreek dat hulle hul heilsame invloed uitoefen deur die weefselreaksies op verskeie 'irriteermiddels' te beïnvloed.

Die opsienbarende ontdekking wat deur Hench en Kendall gedoen is, het gelei tot pogings deur ander ondersoekers om heilsame gevolge by misvormende gewrigsontsteking te verkry deur die gebruik van ander steroïedes, bv. desoxikortone (desoxikortikosterone), progesterone, testosterone, pregnenolene, asetoxipregnenolone ens. In die literatuur daaroor het uitslae wat mekaar weerspreek vinnig opgestapel.

Lewin en Wassen[7] het daarop aanspraak gemaak dat die gelyktydige toediening van desoxikortone en askorbsuur (,ascorbic acid') 'n treffende, vinnige verbetering by misvormende gewrigsontsteking laat intree het. Hulle is op kragtige wyse gesteun deur la Vay en Loxton[8, 9] en deur ander waarnemers in verskeie dele van die wêreld. Die 12 mediese lede van die *Empire Rheumatism Council* van Groot-Brittanje het egter die besliste mening uitgespreek dat hierdie vorm van behandeling van geen waarde vir misvormende gewrigsontsteking is nie. Die grootste meerderheid van geneeshere wat vertroud is met misvormende gewrigsontsteking en met die uitwerking van Kortisone en ACTH het glad nie onder die indruk gekom van die aansprake wat daar gemaak is vir desoxikortone en askorbsuur nie; of van die aansprake vir enigeen van die middels wat hierbo genoem word. 'n Rolprent met le Vay en Loxton as geneeskundige raadgewers, wat handel oor sommige gevalle van misvormende gewrigsontsteking wat met desoxikortone en askorbsuur behandel is, is werklik in Londen aan die Pers vertoon; maar die *Lancet* het

6. Hench, P. S. (1950): Proc. Staff Meet. Mayo Clin., **25**, 474.
7. Lewin, E. en Wassen, E. (1949): Lancet, **2**, 993.
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9. le Vay, D. en Loxton, G. E. (1950): Lancet, **1**, 209.

by the *Lancet*.[10] The paucity of objective evidence was criticized, and the opinion was expressed that the film would not convert any of the sceptics.

Similarly, Davison *et al.*[11] and Freeman *et al.*[12] described improvement in cases of rheumatoid arthritis treated with pregnenolone, but Hench and Kendall and other investigators have found it of no value. At the recent meeting of the American Rheumatism Association in San Francisco, the opinion was expressed by leading members of the Association that as yet no substances except Cortisone and ACTH (with the probable exception of Compound F) can be held to have substantiated their position in the endocrine treatment of rheumatoid arthritis.

There has naturally been much speculation why different investigators have differed so sharply on the efficacy of these steroids in rheumatoid arthritis. The problem is more easily understood if it is recalled that rheumatoid arthritis is a condition in which spontaneous and wide fluctuations may occur. It is well known that a percentage of cases tends to remit to variable degrees over periods of months or years, but, in addition, the severity of the symptoms of the disease may vary from week to week, from day to day, and even from hour to hour (' I'm feeling better to-day, doctor '). Moreover, there is great difficulty in excluding psychological factors in assessing the value of any new form of therapy in rheumatoid arthritis. The performance of the patient, for example, is not only limited by pain and by deformities, but by his willingness and keenness to move the affected joints. There are other cases of rheumatoid arthritis who refuse to yield to invalidism and struggle on with their affliction, endeavouring to work and to enjoy recreation to the best of their ability. They are in a frame of mind in which they are only too ready and willing to feel ' improved ' by various forms of therapy. It is for all these reasons, perhaps, that there has often been such difficulty experienced in interpreting reported results.

10. Annotation (1950): Lancet, **1**, 675.
11. Davison, R. *et al.* (1950): Arch. Int. Med., **85**, 365.
12. Freeman, H. *et al.* (1950): J. Amer. Med. Assoc., **142**, 1124.

ernstig getwyfel aan die verstandigheid om die rolprent vry te stel.[10] Die skaarsheid van objektiewe getuienis is gekritiseer en die mening is uitgespreek dat die rolprent geeneen van die twyfelaars tot ander insigte sou bring nie.

Netso het Davison *et al.*[11] en Freeman *et al.*[12] die verbetering beskryf in gevalle van misvormende gewrigsontsteking wat met pregnenolone behandel is, maar Hench en Kendall en ander navorsers het dit waardeloos gevind. Op die onlangse vergadering van die *American Rheumatism Association* in San Francisco is die mening deur toonaangewende lede van dié vereniging uitgespreek dat daar nie tot dusver beskou kan word dat enige stowwe behalwe Kortisone en ACTH (met die moontlike uitsondering van Verbinding F) hulle plek in die endokrienbehandeling van misvormende gewrigsontsteking verdien nie.

Daar was natuurlik veel bespiegeling oor die rede waarom verskillende ondersoekers in die geval van misvormende gewrigsontsteking so skerp verskil het oor die doeltreffendheid van hierdie steroïedes. Die probleem word makliker begryp wanneer daarmee rekening gehou word dat misvormende gewrigsontsteking 'n kwaal is waarin spontane en groot wisselinge kan voorkom. Dit is alombekend dat 'n persentasie gevalle 'n neiging toon om oor 'n tydperk van maande of jare in mindere of meerdere mate te verbeter maar daarbenewens kan die hewigheid van die simptome van die siekte van week tot week, van dag tot dag en selfs van uur tot uur verskil (‚Dokter, ek voel vandag beter'). Dit is buitendien uiters moeilik om sielkundige faktore uit te sluit by die waardebepaling van enige nuwe vorm van behandeling van misvormende gewrigsontsteking. Die pasiënt se vertoning word byvoorbeeld nie slegs beperk deur pyn en misvormings nie maar deur sy bereidheid en gretigheid om die aangetaste gewrigte te roer. Daar is ander gevalle van misvormende gewrigsontsteking wat weier om aan sieklikheid toe te gee en met hulle siekte aansukkel terwyl hulle probeer werk en na die beste van hulle vermoë ontspanning probeer geniet. Hulle verkeer in 'n gemoedstoestand waarin hulle maar te bereid en begerig is om ‚beter' te voel as gevolg van verskillende vorms van behandeling. Dit is miskien om al hierdie redes dat daar dikwels soveel moeilikheid ondervind is om die aangemelde uitslae te vertolk.

10. Annotation (1950): Lancet, **1**, 675.
11. Davison, R. *et al.* (1950): Arch. Int. Med., **85**, 365.
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ADRENAL CORTICAL HORMONAL AND VITAMIN C THERAPY

A REVIEW

J. DRUMMOND, M.D.
Durban

Hench *et al.* of the Mayo Clinic[1] have directed attention to the benefits of Kendall's fraction E (17-hydroxy-11-dehydrocorticosterone) or cortisone, in the treatment of rheumatoid arthritis. This synthetically prepared steroid has produced most dramatic results, but its general application has been prohibited by expense and its limitation of supply. The natural steroid hormones are equally efficacious in producing remissions in rheumatoid arthritis, when the patient's cortical quantitative output is increased by injections of anterior pituitary corticotrophic hormone (ACTH). This hormone is also in short supply.

Li[2] has obtained a fraction from ACTH which is said to be eight times as active as the original hormone.

Selye [3, 4] has confirmed Hench's findings in experimental formalin-induced arthritis in rats. He satisfied himself that such arthritic change can be prevented or cured by cortisone and by ACTH. He also demonstrated that synthetic desoxycorticosterone (DOCA) injected before or after the induction of rat arthritis intensified the arthritic response.

Wassen and Lewin [5] revived interest in DOCA by announcing that administration of this synthetic steroid to rheumatoid arthritis sufferers, when accompanied by liberal parental dosage of vitamin C (500 to 1,000 mg.) produced prompt and in some cases dramatic remission of the arthritis. This they claimed as comparable to that attained by cortisone and by ACTH.

Landsberg [6] has confirmed the clinical results attained by Wassen and Lewin as have also Le Vay and Loxton,[7] and Landsberg has further announced that testosterone 25 mg. or progesterone 2 mg., when injected in conjunction with vitamin C, have a powerful 'cortisone-like' activity equal, as judged by results to cortisone, ACTH or DOCA and vitamin C.

Brownlee [8] has repeated Selye's researches in rats and confirmed the arthritic response to the injection of formalin. He has been able to convince himself, and those of us who have read his report, that these claims appear to be justified. DOCA alone intensified the arthritic response, but when it was used in conjunction with vitamin C this combination prevented the development of arthritis or produced rapid remission after it had developed. He makes the reservation that full prevention or remission is attainable in normal rats only but not in adrenalectomized ones. This is also the finding with ACTH which, to produce its results, must be able to activate intact adrenal glands.

The intrusion of vitamin C into the controversy at this late date would suggest that the publications of Giroud [9] and Sayers *et al.*[10] had not received the attention they merited when they appeared. They noted that injections of ACTH produced a rapid depletion of vitamin C storage in the suprarenal cortex, rapid depletion of cholesterol and eventual cessation of vitamin C excretion by the animals undergoing research. This ascorbic-depletion is to-day used as a test for ACTH potency. These findings as they apply to ACTH would now seem to apply with equal force to cortisone.

Clinicians using these two agents in the treatment of rheumatoid arthritis have noted with some constancy that in patients who have an open wound or an abscess cavity, healing of the former ceases or granulation tissue formation in the latter fails to occur.

One school of thought is inclined to attribute these happenings to a damaging effect of steroid hormones directed against collagen tissues. This may be so, but one feels that the more acceptable explanation should be that depletion of vitamin C storage as therapy is maintained, deprives the patient of this essential aid to normal tissue repair and healing. From what has been related so far, three conclusions are justified.

i. Cortisone (a synthetic steroid) will, in adequate dosage, produce remission of the signs and symptoms of rheumatoid arthritis.

ii. Natural hormones thrown out by stimulation of the adrenal cortex with ACTH will produce the same happy result.

iii. Some action of vitamin C is embodied in the therapeutic response. Sayers postulated that cortical vitamin C and cholesterol were intrinsically concerned in the generation of steroid hormones.

That hypothesis still fails to solve the conundrum as it applies to DOCA and vitamin C.

Landsberg endeavours to supply the solution by suggesting that the redux potential of vitamin C takes part or is instrumental in generating hydroxy hormones from these members of the steroid group lacking the hydroxy component. Brownlee makes the same suggestion while the writer tentatively claims some priority for having put this thesis forward in a letter to Hench in August 1949 (so far not acknowledged) and repeated in a letter to Selye in January 1950. In his reply the latter was kind enough to say that 'the theory was most interesting and extremely reasonable, but would obviously require confirmation or otherwise by appropriate research'.

Be this so or not, vitamin C has a place in this therapy and clinicians are reminded that any or all aqueous extracts of steroid hormones which are on the market are totally devoid of any content of vitamin C.

Hench would appear to have had his attention directed to the suprarenal cortex by noting remission of rheumatoid arthritis during pregnancy and episodes of jaundice. His choice of cortisone was arrived at by a process of trial and error with suprarenal steroid fractions. There is, however, further support for the adoption of the theory that the suprarenal cortex would supply the answer to the search for the appropriate therapeutic agent if we are also prepared to accept the thesis that the offending agent in rheumatoid arthritis and other allergic reactions is histamine.

In the *British Medical Journal* of 5 March 1947 there is a sub-leader on work carried out by Ungar [11, 12, 13] in connexion with mechanical and toxic injury, summarized as follows:

'Several stages of the argument still need confirmation but it seems probable that normal response to injury is somewhat as follows. The anterior pituitary in response to the stimulus of injury increases its output of ACTH; the adrenal cortex responds with increased activity; the spleen, stimulated by the suprarenal cortical hormones, increases its output of splenin; splenin activates antitrypsin which is present in normal serum, but which is comparatively inert until combined with splenin; activated anti-trypsin decreases breakdown of protein and thus frustrates the release of histamine; and finally the reduction in circulating vaso-dilators such as histamine decreases the bleeding time and capillary fragility and permeability, which are such constant features of histaminic intoxication.

The relationship between these observations and the "alarm reaction" of Selye, and the changes in protein metabolism after injury reported by Cuthbertson [14] and others still need exploration.

It seems not improbable that a new window has been opened through which may be viewed from a fresh angle many problems both of surgery and of general medicine.'

One can readily visualize that Ungar's normal 'chain-reaction' may conceivably break in an abnormal subject at any one of many links, leading to severe and uncontrolled release of histamine. If this be accepted, then the limitations of our therapeutic armamentarium may negative any specific attempt to repair the broken link.

The alternative approach must be to adopt substitution therapy. In doing so we have little or no choice but to make use of adrenal cortical hormones and, furthermore, to combine with them vitamin C. A potent preparation of splenin may supply the ultimate answer. Our primary object would be to nullify release of histamine while leaving the patient to cope with any excess of this protein derivative in his circulation.

At the same time one's personal opinion based on experience is that the addition of synthetic antihistaminics and of vitamin K to the therapy would be of value in preventing further histaminic damage as well as in repairing damage already accomplished. The necessity of such additional therapy will receive some confirmation in case histories to be related.

Selye is inclined to the view that rheumatoid arthritis is a manifestation of an antigen-antibody reaction, the offending agent being histamine and that steroid hormones exercise an anti-histaminic effect in producing remission. Ungar gives us a reasonable explanation of the steps necessary to the control of histamine release.

If these theories, based as they are on exacting and well-controlled research, are accepted, it becomes apparent that the whole field of allergy and allergic reactions is open to therapeutic control. This is probably so because increasing reports from clinicians of repute make reference to cures of asthma, urticaria, lupus erythematosus, ulcerative colitis, peri-arteritis nodosa, etc., attained with adrenal cortical hormones.

Since 1936, when Nayab Farah of Cairo published in the *Lancet* his results in treating enteric fever with adrenal cortical extract and vitamin C, one has been interested in these therapeutic possibilities. This interest culminated in the publication of records of 119 successive cases of enteric fever so treated, with only one death in the series.[15] However, real and sustained interest eventually became established with the realization of the potentialities inherent in treating allergic subjects with steroid hormones. Moreover, as one progressed in theory and practice, it became evident that we should transfer our attention from the obvious as portrayed in the shock organ, to the functional, pathological and metabolic disruptions in other parts of the system of the particular sufferer. It has become more and more established that conditions which at one time were in no sense regarded as allergic reactions were indubitably of this nature.

The researches of Mesugi *et al.*[16] and of Cavelti and Cavelti[17] have shown beyond doubt that acute glomerular nephritis arises as an antigen-antibody reaction and the renal damage makes it self-evident that a rising blood urea must inevitably supervene as a complication. Craig, Clark and Chalmers[18] appear to have proved the theory, if it needed proof, from the therapeutic point of view, by the results they achieved in treating acute glomerular nephritis with a synthetic anti-histaminic preparation—Anthisan. This therapy, however, did not correct the urea retention. A raised or a rising blood urea is a feature of Addison's disease and while we appreciate that it is of extra-renal origin, nevertheless we find that it is dramatically corrected by adrenal cortical hormones. This is also the case in lower nephron nephrosis in which the condition of the patient clinically is in many ways a duplication of that of a case of Addison's disease in a critical phase.

It is fully appreciated that urea in itself is relatively non-toxic, but if it accumulates to excess in the blood stream, and if at the same time urea excretion through the natural renal channels shows evidence of gross depreciation, one feels that one should do something to correct the disparity. The natural assumption would be that if urea is being retained, other and infinitely more toxic substances may be and probably are being retained as well. This assumption applies with equal force whether the azotemia is of renal or extrarenal origin. On the same basis one could reasonably adopt the hypothesis that augmentation of urea excretion when attainable would provide a valuable index of the excretion of other blood-borne toxins; nor is urea retention the only abnormality calling for correction. As research into the allergic reaction progresses, more light is being thrown on other abnormalities.

There is, e.g. evidence of hepatic damage as represented by the frequent finding of a profound depreciation of the blood prothrombin level in allergic persons. This has been repeatedly demonstrated in urticaria and the writer has found it to be so in angio-neurotic oedema and in acute rheumatoid arthritis; nor can we escape the conclusion that in many of these diverse allergic reactive states, there is disturbance of the salt-water electrolyte balance. This is prominent in lower nephron nephrosis, in glomerular nephritis and in acute paralytic ileus, all of which the writer believes to be focal examples of histaminic damage.

We may draw an analogy between urticaria and lower nephron nephrosis. In the former we have a central wheal of pale, oedematous tissue saturated with histamine and surrounded by a red flare. Lewis attributes the flare to be due to dilatation of arterioles in response to an axon-reflex which shunts the blood into these vessels. In lower nephron nephrosis, as so brilliantly portrayed by Trueta and his colleagues, there is a pale, swollen, renal cortex with a shunt of blood from this area into the medullary and juxta-medullary arterioles. This shunt is also attributed to an axon-reflex phenomenon. We advance the suggestion that lower nephron nephrosis could be justly defined as a renal prototype of urticaria.

Now if we are prepared to accept that sodium chloride depletion and urea and potassium retention are features of some, at least, of the allergic states, then the researches of Nichols[19] become of importance. He reported that in rats, deprivation of sodium chloride leads to a gross depreciation of lipids and cholesterol in the adrenal cortices of the experimental animals and to ultimate death. It therefore becomes reasonable to assume that the sodium chloride factor may work in reverse and that any therapy which converts a negative salt balance into a positive one will have beneficial repercussions on the activity of the adrenal cortex. We have overwhelming research confirmation of this.

The full comprehensive systemic picture of the allergic reaction is well summarized by Bergstrand[20] in his dissertation on hypersensitivity reactions:—

'I should like to stress the importance of correlating our clinical, serological and pathologico-anatomical knowledge of

these problems better than in the past. The theory that the great number of clinical entities that I have mentioned here are only anaphylactic tissue reactions, would then perhaps not be relegated to the world of fancy, as now quite often happens.'

With this comprehensive picture we can exploit such therapeutic measures as we know will adjust the abnormalities. We have already adduced some proof that cortical steroid hormones are vitally concerned in the nullification of histamine release. They are equally vitally concerned in the regulation of the salt, water and electrolyte balance of which activity no better example can be put forward, than Addison's disease. Li [2] in listing the activities of cortisone and ACTH states: 'They promote excretion of nitrogen and potassium and retention of sodium chloride.'

This particular property of steroid hormones as it applies to excretion of urea and potassium would appear to be due to some selective stimulation of glomerular filtration and operates whether the intra-glomerular blood pressure is high or low. Research on Addison's disease is confirmatory of this and the writer has put it to the test in a case in which the patient's blood pressure was 225/120 mm. Hg. The blood urea was found to be 98 mg. per 100 c.c. and the urea excretion 21% of normal. After two weeks of intravenous daily injections of 5 c.c. cortical extract mixed with 500 mg. of vitamin C, the tests were repeated. The blood urea was now found to be 32 mg. per 100 c.c. and urea excretion 176% of normal.

Cortical steroid hormones would appear, therefore, to be our therapy of choice in all conditions in which histamine intoxication is operative, urea excretion impaired and salt-water-electrolyte balance disordered. Furthermore, their administration should always be combined with full dosage of vitamin C. Therapeutic potentialities in the genito-urinary field are unlimited.

It is now proposed to present details of actual cases in which all the points referred to will be given due value and prominence.

GLOMERULAR NEPHRITIC CASES

Case 1 (*Referred by Dr. L. Pearson*): Miss M. R. *aet.* 22 came under my care in October 1945. She had had a sub-total thyroidectomy performed in 1937 and remained well for the subsequent five years. She then sought advice while in Johannesburg for a rapidly progressive haemorrhagic diathesis of indeterminate origin. The picture comprised haemoptysis, haematemesis, haematuria and metrorrhagia.

Diagnosis after very thorough investigation was decided upon as acute haemorrhagic nephritis.

Urinary findings were typical: blood urea, 98 mg. per 100 c.c.; urea excretion, 24% of normal.

Blood count: 2.4 million red cells per mm.; 8.4 gm.% Hb. Chief supportive treatment for the next four years consisted of repeated blood transfusions of which she had more than 20. She then transferred to Durban and came under my care. She was admitted to a Nursing Home and blood was taken for routine investigation. On the same day she had a series of uraemic convulsions lasting an hour.

Blood: Red cells, 1.2 million per c.mm.; Hb, 27%; blood urea, 138 mg. per 100 c.c. She was given a pint of blood on three successive days without incident and with considerable apparent benefit.

The protean nature of the haemorrhages which were coming from lungs, kidneys and uterus suggested a generalized state of capillary fragility possibly resulting from an antigen-antibody reactive background. It was decided, therefore, to try the effect of suprarenal cortical extract and vitamin C and a daily intravenous injection of 10 c.c. cortical extract mixed with 500 mg. vitamin C was begun. From the commencement of this therapy (26 October 1945) no further transfusion of blood became necessary for the ensuing three years.

Within two weeks all evidence of haemorrhage had disappeared except some persistent uterine oozing. This ceased after three daily injections of progesterone and suggests that Landsberg was right when he noted the 'cortisone-like' action of this hormone when given with vitamin C.

During the treatment, interval blood urea levels fell from 138 mg. to 38 mg. per 100 c.c. and urinary nephritic findings became negligible. She resumed and maintained a normally active life although the frequency of injections was eventually reduced to bi-weekly instead of daily.

An attempt to anticipate suprarenal cortical atrophy said to eventuate in subjects receiving natural hormones, was made with ACTH kindly supplied by Organon Ltd., London. It had no appreciable effect and the makers informed me subsequently that this particular batch of the pituitary hormone had been retested and found to be inert.

In October 1948 a sudden and marked deterioration set in with reappearance of haemorrhagic manifestations. She was found to have a blood urea of 98 mg. per 100 c.c. and in spite of intensification of therapy and further blood transfusion, she sank into uraemic coma and died within one week of the onset of the relapse.

She had been given three years of reasonably normal enjoyment of health before the damage became reactivated and irreversible. It is probable that her own intrinsic cortical activity failed.

Case 2 (*Referred by Dr. A. Bloom*): Mr. M. L. a Greek aged 42, was placed in my care in January 1947 as a presumably hopeless case. He had gross ascites and massive oedema of the legs and scrotum, the latter as large as a football. The blood pressure was low; blood urea, 108 mg. per 100 c.c.; total 24 hours urinary output was only 6 to 8 oz. It contained a heavy cloud of albumin with hyaline and granular casts microscopically. Paracentesis of the abdomen was necessary and 25 pints of clear fluid were removed. An attempt to promote diuresis with a mercurial diuretic and vitamin C elicited no response and for the ensuing two months repeated paracenteses at 10-day intervals were required. On each occasion 25 to 30 pints of fluid were recovered. It was then decided to try the effect of cortical extract and vitamin C injections alternating each day with the mercurial drug and vitamin C. This was because of an experiment conducted by Gaunt and recorded by Soffer [21] to the effect that if water be injected intra-peritonealy into adrenalectomized dogs, it is all retained, but that if cortical extract is administered it is totally and promptly excreted.

For eight days no increase in diuresis was manifested in excess of 8 oz. per 24 hours, but he then had an output of 86 oz. From this date onwards profuse diuresis was maintained on the above therapy and no further paracentesis became necessary. Oedema and ascites diminished steadily and ultimately vanished completely after three months' treatment. The urine became albumin free and the blood urea fell steadily from 108 mg. to 38 mg. per 100 c.c. by August 1947. He became active and ambulant and took ship for his home in Athens in October 1947, still on the same treatment and taking supplies for continued therapy with him. He has reported well in several letters since, the last in December 1949, but has given no recent indication whether he has had to persist with the treatment or not.

Case 3 (*Referred by Dr. M. Hulett*): Miss H., *aet.* 35, matron of a Nursing Home, had had an abscessed tooth removed with local anaesthesia on 11 March 1949. Four days later she awoke with gross oedema of the face, hands, legs, etc., of acute nephritic type, and associated with severe cramps in both legs. Her urinary output for the previous 24 hours had been only 6 oz. Her urine showed trace of albumin and an occasional red blood cell. This suggested that at this early stage the glomeruli had not as yet frankly broken down. The blood urea was 43 mg. per 100 c.c.

Treatment with cortical extract and vitamin C was instituted forthwith and within four days the oedema had completely vanished and no cramps were being experienced. The urinary output had moved up to 64 oz. in 24 hours and chemically

and microscopically no abnormality was detectable. The blood urea had fallen to 33 mg. per 100 c.c.

On cessation of treatment after three weeks, a relapse occurred which came rapidly under control with resumption of therapy. This relapse was explained when dental X-ray revealed numerous dead teeth with root abscesses and we had every reason to hope our difficulties were solved when these were removed under penicillin control.

She remained well for a lengthy period and then irregular bouts of oedema recurred. Renal function was normal on all appropriate tests and on the assumption that the shock organ had shifted from kidney to skin, blood prothrombin levels were determined. Two records on successive days from two different laboratories returned the identical figures of 0.0% of normal. Vitamin K rapidly brought the figure up to 98% of normal with some, but incompletely sustained, benefit. On the assumption that a streptococcal antigen-antibody reaction was still operative, an attempt is now being made to desensitize her with a course of haemolytic streptococcal vaccine. Reactions to injections would suggest that success is in the offing. Bergstrand makes a feature of the differences which exist as between simple anaphylaxis and organismal sensitivity and they would appear to resemble the type encountered in this case.

LOWER NEPHRON NEPHROSIS

This catastrophic condition, which can arise from such an infinite variety of injuries, traumatic and infective, has not as yet had its etiology clarified. It can present as a complication of crush injuries, extensive burns, pneumonia, meningococcal septicaemia, anaphylactic shock, sulphonamide medication, coronary thrombosis, etc. This suggests that there is some common factor which acts on the renal mechanism and function with such devastating results.

Some accept histamine as the damaging agent, and adduce evidence of gross impairment of suprarenal cortical function as part of the picture. Haemorrhage into the adrenal cortical tissues leading to total destruction has been frequently recorded. A mounting weight of evidence suggests that administration of cortical hormones benefits the sufferers, though in all fairness it must be stated that these claims are denied by other investigators.

In all the literature one has studied there has been no single mention of the hormones having been exploited in conjunction with vitamin C. There would obviously appear to be some simpler approach in therapy than to be obliged to have recourse to the artificial kidney, peritoneal lavage, gastro-intestinal suction, etc., and the following case histories may therefore be more than purely informative.

Case 1 (*Referred by Dr. Eric Deale, January 1949*): Mr. M. had undergone an operation which necessitated the removal of large masses of pathological omentum from the upper abdomen. He had been a free drinker and was a mild diabetic. No cause for the condition was noted at operation but the terminal illness suggested that it was malignant. Following operation he had severe and prolonged vomiting which persisted in spite of intravenous saline therapy and other appropriate remedies.

On the eighth post-operative day, diarrhoea occurred, and three days later he developed continuous and exhausting hiccough. The urinary output had fallen to 4-6 oz. in 24 hours. Blood urea estimation at this stage recorded a figure of 245 mg. per 100 c.c.

The condition on examination was as described above with the added finding that the strain of vomiting had burst his wound open to the peritoneal layer. The prognosis appeared to be hopeless but it was agreed, on the basis that lower nephron nephrosis with uraemia was present, to try the effect of cortical hormones and vitamin C in full dosage of 10 c.c. and 500 mg. each daily.

Vomiting and purging ceased in three days and hiccough the following day. On the fifth day of therapy the blood urea had dropped to 42 mg. per 100 c.c. and the urinary output had risen to 68 oz. in 24 hours. The critical loss of chlorides, which is a feature of a vomiting patient, was almost certainly controlled by the therapy. Convalescence on therapy was uninterrupted and two weeks later wound was re-closed and healed by first intention.

I saw this patient three months later with signs and symptoms of a cerebral tumour. He was referred to Mr. Krynauw in Johannesburg and died after an operation which revealed metastatic carcinomatous secondary deposits in the brain.

Case 2 (*Referred by Mr. A. Radford*): Mr. v. d. L., *aet.* 68, was submitted to operation on 18 January 1950 for extensive diverticulosis of the colon. A wide resection of affected bowel was carried out and an anastomosis and a right sided colostomy established. I did not see him until later on and am indebted to Mr. A. Radford and Dr. H. Grant Whyte, the anaesthetist, for notes on the case at this stage.

He was obviously shocked by the operation and his condition deteriorated rapidly with the appearance of progressive oliguria (in spite of intravenous saline), hiccough and other signs of uraemia.

Six days after operation the blood urea was 110 mg. per 100 c.c. and two days later 150 mg. per 100 c.c. with urea excretion 1.14. At this stage the anaesthetist has since informed me that the case had been technically 'written off'. Treatment with cortical hormones and vitamin C was begun.

Response to therapy was immediate and sustained. One week later the blood urea was 55 mg. per 100 c.c., diuresis well established and therapy was discontinued probably prematurely.

On 10 February I saw him on my return from leave with a view to preparing him for closure of his colostomy. The blood urea was 68 mg. per 100 c.c. and therapy was re-established. One week later the blood urea was 29 mg. per 100 c.c. and the operation was carried out with satisfactory closure and healing. Further therapy on a modified scale enabled him to leave the Nursing Home two weeks later. When seen on the race course three months later, he appeared to be fit and well and pronounced so himself.

The lesson to be learned from this case is that intelligent pre-operative preparation and post-operative follow-up with steroid hormonal and vitamin C therapy might banish this dread complication from major surgery.

Case 3 (*Notes supplied by Dr. Addleson*): Mr. H., *aet.* 57, was admitted to Entabeni Nursing Home on 18 June 1949 with a diagnosis of left lower lobar pneumonia and signs indicating myocardial and renal failure. He was drowsy and in muttering delirium. The tongue was dry, brown and furred. The prostate was not enlarged. No oedema. Blood pressure, 160/40 mm. Hg. Blood urea, 208 mg. per 100 c.c.

He was put on to intensive interval doses of penicillin on the day of admission with a total dosage of 400,000 units per 24 hours. Case notes now follow:—

19 June. Patient drowsy, stuporous and hiccoughing. Catheter was passed 36 hours after admission as no urine had been voided naturally. 9 oz. of urine were recovered; 5 c.c. cortical extract and 500 mg. vitamin C were given in the evening and repeated night and morning for the following six days.

20 June. Condition critical but 28 oz. of urine were voided naturally during the 24 hours. This increased to 64 oz. in the next 24 hours.

22 June. Patient much improved. No hiccough for 24 hours. Condition alert and cheerful. Urinary output, 76 oz. Only a trace of albumin present. Subsequent progress on above therapy was sustained and patient was discharged on 4 July, 16 days after his admission to Hospital.

No further blood urea estimation was done, but there would be every justification in assuming that a lower nephron nephrosis developing as a complication of lobar pneumonia had been dealt with successfully.

Case 4 (*Referred by Dr. Bassa*): Mr. R., *aet.* 42, an Indian patient, was seen in consultation with his medical adviser on 8 February 1949. The history was that two days before he had had an attack of pain of severe degree, located substernally and radiating to both arms. It was clinically typical of coronary occlusion.

When first seen he was badly shocked and collapsed, and this state persisted in spite of liberal dosage of morphine and coramine. Two days after the onset of the illness, I was asked to see him.

My first impression was that he was likely to die at any moment. He was comatose with Cheyne-Stokes breathing. The pulse was fluttering and almost imperceptible. Rate was approximately 120 per minute. The blood pressure could not be recorded, an occasional faint sound being heard at 60 mm. Hg. There had been anuria for 24 hours.

During the course of examination he had two convulsive attacks in each of which the pulse disappeared and one feared that death had ensued. A diagnosis of coronary thrombosis with secondary lower nephron nephrosis was agreed upon and although the prognosis appeared hopeless, it was decided to attempt resuscitation with cortical extract and vitamin C to be given twice daily in full dosage of 10 c.c. and 500 mg. each.

I was asked to see him again two days later and was agreeably surprised to find him not only alive but conscious and alert. He had recovered consciousness several hours after his initial injection when he also voided 12 oz. of urine. This output had risen to 72 oz. during the 24 hours preceding my return visit. The blood urea at this stage was 78 mg. per 100 c.c. The pulse was strong and regular and the blood pressure was 108/70 mm. Hg.

The same therapy was advised with control of salt intake but not full deprivation. He maintained improvement for a further 10 days to such a degree that it became difficult to keep him resting in bed. In one of his unauthorized excursions out of bed he suddenly collapsed and expired in a few minutes, presumably as the result of overtaxing his damaged myocardium.

The resuscitation of this patient was the most impressive tribute to the therapy and his subsequent demise the most disappointing feature of the case.

ACUTE PARALYTIC ILEUS

As this catastrophe is a post-operative histaminic bowel effect, it should be not only curable but preventable.

On the theory that certain organisms in a putrefactive setting generate histamine in the bowel from histidine by a process of splitting off CO_2 (Starling [22]), and that the released histamine sets in train the development of acute paralytic ileus, steroidal hormone therapy should prove efficacious.

Many of these cases terminate with the added complication of lower nephron nephrosis and it is interesting to note that Hueur and Andrus [23] have produced the shock syndrome in animals by injecting into them fluid from closed intestinal loops.

In acute paralytic ileus the gravity of the condition of the patient is aggravated by loss of sodium chloride in the vomitus and with suction. If treatment is to be successful, the lost sodium chloride must be replaced and retained. Gross loss must inevitably lead to adrenal cortical hypofunction and when this happens absorption of sodium chloride from the bowel ceases.

The clinician should therefore replace sodium chloride parenterally and ensure its retention by administering cortical hormones which at the same time will exert anti-histamine activity.

Case 1 (*Treated and Notes Supplied by Dr. Addleson*): Dr. H., a country practitioner, came under the care of Mr. Radford who formed a provisional diagnosis of acute haemorrhagic pancreatitis. The urine showed 3% sugar. Operation took place on 24 May 1949. The provisional diagnosis was confirmed and owing to the poor condition of the patient the abdomen was closed without further surgical interference.

The patient was put on to intravenous saline drip and sedatives and his post-operative treatment was undertaken by Dr. Addleson. His notes record:—

27 May 1949. i. Patient suffering from post-operative acute paralytic ileus.

ii. Urinary output reduced to a few oz. in 24 hours. It contained sugar ++; acetone +.

iii. Temperature 101° F. Pulse, 108 per minute; respiration, 24 per minute.

iv. Patient extremely restless and ill. Tongue dry and brown. Persistent hiccough present. Bowels confined. Mentally alert.

v. He had been on intravenous saline and gastric suction since operation three days previously.

This treatment was continued plus insulin, penicillin and to this was added 10 c.c. cortical extract and 500 mg. vitamin C which were introduced into each Vacoliter.

29 May 1949. Patient greatly improved. Skin moist. Urinary output greatly increased. Hiccough has ceased. Abdominal distension greatly reduced and flatus being passed freely.

31 May 1949. By this date abdominal distension had completely disappeared. Urinary output now normal and showing no sugar or acetone. A good bowel action recorded.

1 June 1949. Suction and therapy discontinued.

Subsequent convalescence was uninterrupted and patient left the Nursing Home 16 days after his operation.

He is to-day back on duty in his practice in Northern Natal and very well.

Case 2 (*Case Notes Supplied by Dr. Addleson*): Mr. D. was operated on by Mr. Pearson in Entabeni Nursing Home, a first stage Smithwick splanchnicectomy being performed for hypertension. This was on 25 May 1949. For several days he progressed satisfactorily and then began to show evidence of acute paralytic ileus. His treatment was undertaken by Dr. Addleson with whom I had discussed at various times, my theories. His notes read as follows:—

25 May 1949. Operation, lumbar sympathectomy.

30 May 1949. Seriously ill with marked degree of acute paralytic ileus. On this day he was started on intestinal suction and intravenous saline drip.

1 June 1949. Abdomen more distended and tense. Urinary output a few oz. only. Skin dry. Tongue dry and brown. Temperature 100° F. Penicillin added to therapy.

2 June 1949. Patient going down-hill fast and prognosis desperately poor. 5 c.c. cortical extract and 500 mg. vitamin C introduced into each Vacoliter.

3 June 1949. Dramatic improvement. Considerable increase in output of urine. Abdominal distension much reduced. Patient much more alert.

6 June 1949. Suction, intravenous drip and all other therapy were discontinued as result of total disappearance of abdominal distension coinciding with resumption of bowel action and normal urinary output.

He was able to leave the Nursing Home fully recovered from his post-operative illness. In view of the almost catastrophic sequel to the first stage of his operation, the second stage was reluctantly considered inadvisable.

He is reported to have succumbed to an attack of coronary thrombosis in Johannesburg one month later.

These two cases, while not proving the theory, at least do appear to suggest that further trial of the method is called for. Furthermore, and what is more important, they suggest the advisability of preparing patients for such operations by preliminary administration of steroid hormones and vitamin C, and continuance of such therapy post-operatively. Acute paralytic ileus can arise in circumstances quite unconnected with surgical insult and we think it does so in persons who have bowel flora which will permit an antigen-antibody reaction or histamine release. As we have no means at our disposal by which we can pin-point these cases, a more general employment of natural systemic anti-histaminics plus chemotherapy would appear to be a wise measure to adopt.

RHEUMATOID TYPE OF ARTHRITIS

If this condition is an allergic reaction, then we will have to add certain additional findings to the triad which

has hitherto been accepted as representing the allergic response, viz.:

(a) Stimulation of smooth muscle.
(b) Increased capillary fragility.
(c) Diminution of blood coagulability.

Suggested additions are:—

i. Interference with hepatic function as indicated by a lowering of the blood prothrombin level.
ii. Diminution of urea excretion with retention of urea in the blood stream. This is probably due to diminished glomerular filtration.
iii. Systemic depletion of vitamin C as recorded by Rinehart [24] in rheumatoid arthritics.
iv. Elevation of the basal sedimentation rate.
v. A tendency to eosinophilia.

Realization of this more comprehensive picture will strengthen the hand of the clinician in carrying out curative therapy, as will be brought out in case histories to follow.

Case 1 (*Seen in Consultation with Drs. J. Hollings, Lewer Allen, B. Moshal and R. Elsdon-Dew*): Master H. J., *aet.* 14, a boy of great athletic promise, developed a sudden severe pain in the region of the right hip. There was associated pyrexia. The leucocyte count was 15,000 per c.mm. with polymorphs 83% and B.S.R. of 103.

A provisional diagnosis of acute osteo-myelitis was adopted and intensive treatment with penicillin was instituted with little or no apparent therapeutic benefit. During the ensuing 10 days pain developed successively in the left hip region, then in the left elbow and finally in the left ankle which became red, swollen and excessively tender to touch.

A revised diagnosis of an acute rheumatoid type of arthritis was adopted.

The blood pressure was 140/82 mm. Hg, a high figure for a boy of 14. Dr. Elsdon-Dew kindly carried out certain additional investigations we were interested in having done. The blood prothrombin level was found to be only 30% of normal. Chemically and microscopically no abnormality was detectable in the urine, but the blood urea was recorded as 46 mg. per 100 c.c. He was given 5 c.c. cortical extract with 500 mg. vitamin C intravenously daily. To this therapy was added vitamin K 10 mg. orally b.d. and one Anthisan tab. t.i.d. Penicillin was omitted.

After three days of this therapy all local and constitutional evidence of arthritis had vanished at which stage B.S.R. was 11, leucocytes, 7,600 per c.mm. and prothrombin level 71% of normal. The blood urea estimation was not repeated but one is confident it would have been normal. He was able to return to his home several days later and when heard of several months later, he was well and active and had had no recurrence of his malady.

I have formed the opinion that as rheumatoid cases have as part and parcel of their illness a depreciation of vitamin C storage, and as ACTH demonstrably reduces this still further and cortisone would appear to do so, relapses which follow discontinuation of these two therapeutic agents are in some way inseparably bound up with vitamin C lack.

The therapeutic prevention of such relapses would on such a hypothesis appear to be simple, i.e. to follow up with parenteral vitamin C for some time. It is possible that by doing so the patient would make his own cortisone although in doing so it is also possible that he would continue to draw on his vitamin storage.

Case 2 (*Referred by Dr. McLennan*): A Police Sergeant S. J. was referred to me on 8 January 1950. He had had an infective skin lesion in the axilla for which he was given several daily injections of penicillin in oil and bees-wax. On the day following the final injection he developed angio-neurotic oedema of the face, trunk, arms and legs of extremely severe degree. At the same time wrist, knee and ankle joints became swollen and excruciatingly painful; a state of affairs as regards the joints which in my opinion was clinically indistinguishable from acute rheumatoid arthritis. Two injections of adrenalin had no effect in relieving his distress and he was put in a Nursing Home and transferred to my care. He was extremely ill. Temperature, 101° F. The oedematous patches were gross in size and the joints excessively swollen and painful. He was put on to vitamin K and Anthisan immediately, but before doing so blood was taken for appropriate tests. B.S.R. was 85. Blood urea, 56 mg. per 100 c.c., and blood prothrombin level 38% of normal.

On the following day and before blood findings were known oedematous effects were found to have subsided although all the joints were still swollen and painful. Therapy with vitamin K and Anthisan was therefore continued. The angio-neurotic oedema flared up with redoubled violence during the ensuing 24 hours and temperature rose to 104° F with no improvement in the joints. It was therefore decided on the assumption that this arthritic complication was probably the purest example of the acute rheumatoid type we ever encounter, to add to his therapy steroid hormone and vitamin C. In view of the claims advanced by Wassen and Lewin, their method was adopted. DOCA 5 mg. in sesame oil was administered into the buttock and 500 mg. vitamin C intravenously daily plus Anthisan and vitamin K orally.

Improvement was immediate and sustained and within 48 hours all evidence of skin and joint involvement had disappeared with return of a normal temperature.

After three further daily treatments he was permitted to return home and when heard of two months later, had had no further recurrence of his malady.

One regrets that it was not possible to repeat the various blood tests in this case, as the expense of such scientific control was not authorized by the Police department.

The perfection of the therapeutic response would suggest that in this case, as in Case 1, the functional hepatic and renal disturbance had been satisfactorily adjusted.

It will be noted that, although reference has been made to disturbances of the electrolyte-water balance in this paper, no attempt has been made to consider this aspect of our problem in detail. The field which covers the question in all its ramifications is a vast one. The one and only point one would wish to emphasize is that if sodium lack and potassium excess are features of an illness, parenteral administration of adrenal

hormones and sodium chloride will aid in the adjustment of the imbalance.

Furthermore we should for the purpose use for preference whole cortical extract or fractions other than the hydroxy ones. The sodium-retaining powers of hydroxy compound fractions is only 1/30 of those not containing the hydroxy component.

Adrenal hormones, for so long neglected, would appear to be coming into their own, but as Hench indicates in his comments on results achieved in rheumatoid arthritis: 'These results but represent the end of the beginning in a new and much wider field of therapy.'

I wish to place on record my appreciation of the help given to me by numerous colleagues; by permitting access to their cases and by their helpful criticism at all times they have been most encouraging.

The research, if it may be so called, is in many respects incomplete and possibly crude. My only excuse for manifest shortcomings in this paper is that when one is dealing with a life which is desperately endangered, short-cuts have to be taken if the life is to be saved.

The excuse one regards as a good one even though the explanation be poor.

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INTRAVENOUS PROCAINE HYDROCHLORIDE

EXPERIENCES IN THE BANTU

MOLLIE B. BARLOW, M.B., CH.B.*
CHARLES WIGDEROW, B.SC., M.B., CH.B., D.A.†
Coronation Hospital, Johannesburg

During the last five years we have used procaine hydrochloride for a variety of conditions, mostly in Bantu, but also in Coloured or Indian cases. Five obstetrical cases were Europeans.

It is more difficult to assess the analgesic value of Procaine in the Bantu as he is stoical and complains less of pain than the European. It is also more difficult to recognize the symptoms of over-dosage or increased sensitivity, partly because of language difficulties and partly because the recognition of flushing of the skin or engorgement of the eyes is not easy in the Bantu.

Chemistry. Procaine hydrochloride or diethylamino benzoate belongs to the alkaline ester group of compounds. These compounds may reveal as their main action either an atropine-like, a curare-like, an antihistaminic or a local anaesthetic reaction (Ing *et al.*, 1945). At the same time they may show, to a greater or less degree, several of the other actions as a side effect.

Clinically, intravenous Procaine has a powerful effect in relieving pain. Procaine, when injected intravenously, concentrates seven to eight times more in the inflamed tissue than in the normal. This is especially so when Procaine is administered with considerable fluid.

* Senior Anaesthetist.
† Assistant Anaesthetist

Fate of Procaine in the Body. Procaine hydrochloride is almost completely metabolized in the body. Until recently, the liver was generally accepted as the principal site for Procaine destruction. Brodie *et al.* (1949) have postulated, however, that the Procaine is mainly broken down in the blood plasma. Clinically, this would appear to be so, for we have found that the Bantu, who show a high incidence of liver damage (Gillman and Gillman, 1948) tolerate Procaine well.

We have used Procaine Hydrochloride in six different ways:

1. As an adjunct to anaesthesia;
2. As the sole anaesthetic agent;
3. For its effect on circulation and shock;
4. As an analgesic;
5. For obstetrics;
6. For therapy.

1. AS AN ADJUNCT TO ANAESTHESIA

Here the Procaine was used either with Pentothal or with nitrous oxide and oxygen. Much work has been done, particularly in America, on the Pentothal-Procaine combination for anaesthesia. We felt that many of the writers were using Pentothal rather than Procaine to obtain their effect, and with this in mind concentrated on increasing the amount of Procaine rather than of Pentothal.

Solutions of Procaine Hydrochloride have an acid pH; therefore, solutions of Procaine Hydrochloride, added to solutions of Pentothal Sodium, lower the pH of the Pentothal Sodium. If the pH of the resulting solution falls below 10, a precipitate of insoluble Pentothal immediately forms and remains.

Allen *et al* (1948) have reported a similar occurrence in their experiments. They found that the precipitate formed by the Procaine-Pentothal combination had no ill-effect on animals. We have substantiated this in human beings.

After the first few cases, we arrived at the conclusion that the optimum amounts to use were as follows:— 0.5 gm. Pentothal, together with 2 or 3 gm. Procaine Hydrochloride in 1,000 c.c. of isotonic saline, or glucose 5% in isotonic saline.

The mixture must be well shaken. A higher percentage of glucose is apt to form a precipitate, but may be used. We do, however, vary this combination when necessary. Case 1 is an example of this.

We would like to emphasize here that the Pentothal is used as an anti-convulsant and not for its sedative or anaesthetic effect.

The drip is run at approximately 60 drops per minute. If, for any reason, it is necessary to run the drip slower or faster, the amount of Procaine may be increased or decreased. Up to 5 gm. of Procaine will mix with 0.5 gm. of Pentothal without forming a precipitate.

We have had our Procaine prepared in 20% and 50% strengths, in 10 c.c. ampoules.

Because Richards (1947) has shown that vitamin C deficiency increases the liability to Procaine toxicity, particularly in the elderly and poorly nourished patient, we feel that in this type of case it is advisable to add 1 gm. of vitamin C to the drip.

We have found that this combination of Pentothal-Procaine minimizes the amount of other and more toxic anaesthetics used. This is of great advantage in debilitated patients. We do not feel that this combination is a substitute in the healthy individual for nitrous oxide, oxygen and Pentothal.

When Procaine is first administered, the patient experiences a sensation of warmth throughout the body. This feeling is accompanied by a feeling of relaxation. Increasing the dosage is followed by 'pins and needles' of the hands and feet, dizziness and talkativeness. If the Procaine is pushed beyond this, the patient may lose consciousness, while if he is sensitive to the drug he may develop twitching and convulsions before losing consciousness.

It is imperative to test all patients who are not under a general anaesthetic for their reaction to Procaine. This may be done by injecting two to three minims of Procaine 1% intradermally. The patient's pulse is then taken every 15 minutes for an hour. A rise of over 10 in the pulse rate is considered to indicate sensitivity.

We feel that a quicker method is to inject 0.25 c.c. of 1% Procaine intravenously, asking the patient to report any signs of dizziness. At the same time, anxiety, sweating or any departure from normal is looked for. After 30 seconds, another 0.5 c.c. is given. If there are no ill effects after a further 30 seconds, another 1 c.c. is given. If there are still no ill effects, the Procaine can be given slowly to the patient. If the patient appears more sensitive than normal, the rate of the drip or the rate of injection is modified accordingly. Too rapid administration in a sensitive patient is liable to produce convulsions. We are indebted to Dr. Schmahmann (1950) for the intravenous testing method.

Our cases have included traumatic amputations, plantar warts, straightening of contractures following burns and indolent ulcers for skin graft. We have not used it to potentiate anaesthesia for abdominal work.

The following cases illustrate the type of operation in which Procaine is useful. It is of interest to note that in Case 1, the only supplementary anaesthetic used was infiltration of the skin with 1% Procaine.

Case 1. A debilitated Coloured woman aged 87 years, with chronic bronchitis, was to have an open reduction of a fractured femur and application of a Smith-Petersen pin.

Premedication: Nembutal gr. 1½. Just before commencement of operation she was put on to a vacolitre drip containing 1,000 c.c. of 5% glucose with 1 gm. of Pentothal, 1 gm. ascorbic acid, 2 gm. Procaine Hydrochloride. The skin incision was infiltrated with a few c.c. of 1% Procaine. The drip was run at 60-80 drops per minute, 500 c.c. being given in 100 minutes. Analgesia was excellent throughout. The pulse varied from 100 to 110 and the patient was returned to the ward in a satisfactory condition.

Case 2. A very nervous Bantu female, aged 14 years, was to have a Smith-Petersen pin removed by open operation, under screening.

Premedication: Omnopon gr. ½ and Scopolamine gr. 1/150th, was given too late and was therefore ineffective.

She was induced with Pentothal, and carried on nitrous oxide 70% and oxygen 30%. A 5% glucose in saline drip, containing 2 gm. of Procaine Hydrochloride and 0.5 gm. of Pentothal was set up.

During the operation, which lasted two hours, she was given intermittent doses of Pentothal. In all, she had 1.4 gm. of Pentothal and 1.35 gm. of Procaine Hydrochloride. She was completely conscious at the end of the operation.

2. AS THE SOLE ANAESTHETIC AGENT

Here the Procaine was given in a 1% solution, i.e. 10 gm. per litre of fluid. The drip was run rapidly (120 to 180 drops per minute) until the patient became unconscious. At this point the drip was slowed to the amount needed to keep the patient anaesthetized. As Pentothal was not used there was a tendency to convulsions.

After using Procaine thus for small cases (e.g. dilatation and curretage, compound and simple fractures) we decided that the anaesthesia obtained was not compensated for by the risks involved and we did not pursue this line of research any further.

We have not used the intermittent method as described by Dr. Schmahmann, and whilst agreeing with him that the risk of convulsions would be considerably reduced by this method, we still feel that Procaine, *per se*, has no place as an anaesthetic.

It is of interest that Allen, who in 1946 reported with others the use of Procaine for general anaesthesia, and who at that time was trying to establish 'an adequate basis for the acceptance or rejection of Procaine as an anaesthetic', stated in 1948, after animal experimentation, that 'whilst retaining Procaine for intravenous analgesia, he had abandoned its use for general surgical anaesthesia, because of rare

unpredictable collapse without convulsions and without known means of prevention'.

An anaesthetic, to be universally used, must be as safe as possible or have a use that justifies the risk involved. We do not feel that Procaine as an anaesthetic fulfils this requirement.

3. FOR ITS EFFECT ON CIRCULATION AND SHOCK

Here Procaine is one of the most useful drugs at the disposal of the anaesthetist. Burnstein (1946, 1949) first described the action of Procaine on cardiac rhythm, and the consensus of opinion would now appear to be that Procaine has a quinidine-like action on the auricle of the heart. With this in mind, we have used it for controlling the arrhythmias arising during thoracic and cardiac surgery.

A 0.2% solution of Procaine is used, i.e. 2 gm. of Procaine per 1,000 c.c. of saline, blood or plasma, and the drip is allowed to run at whatever speed is necessary to maintain the patient's blood pressure or as the exigencies of the operation demand.

When arrhythmias suddenly arise, 50 to 150 mg. of a 1% Procaine solution are immediately injected intravenously. This is repeated when necessary. We have never had occasion to repeat the injection more than three times, generally not more than once. In addition, in certain types of thoracic or cardiac work, where there is liable to be vagal stimulation, Procaine is swabbed over the hilum of the lung or over the pericardium.

The following cases are illustrative of the use of Procaine in arrhythmias and in thoracic work:

Case 3. A Bantu woman aged 30, with jaundice of unknown origin, was to have a laparotomy. She was extremely ill and had multiple venticular extrasystoles. Her temperature was 104.2° F. The anaesthetic was Cyclopropane, d-tubocurare and oxygen. A 5% glucose drip was run during the operation. From the commencement of the operation her pluse was irregular, and after 25 minutes she was given 100 mg. of 1% Procaine intravenously; five minutes later her pulse was regular. After a further 15 minutes it was again irregular, and the Procaine was repeated. Her pulse became and remained regular for another 50 minutes, when the operation ended. As soon, however, as the patient regained consciousness, she became markedly cyanosed and her pulse became grossly irregular. The Procaine was repeated but this time had no effect whatsoever.

Case 4. During pneumonectomy, whilst the bronchus was being ligatured, the patient's pulse suddenly disappeared, the heart itself showing only an occasional beat. The heart was bathed in 1% Procaine and 100 mg. of 1% intravenous Procaine was given. The heart recommenced beating and the blood pressure reappeared.

It was found, in cases of severe shock following trauma, that the addition of 2 gm. of Procaine to the intravenous drip (saline, whole blood or serum) raised the blood pressure. Schmahmann (1950) has found during analgesia with Procaine that the blood pressure was raised. This action, together with the elimination of pain and the anti-spasmodic action of the Procaine on the vein itself. all make the action of Procaine in the drip of value in shock.

4. USE AS AN ANALGESIC

It is here that we feel that Procaine has one of its widest uses:

(a) *Dressing of Burns.* We have used it in approximately 50 cases of burns. These patients are very often greatly shocked and in extreme pain, not all of them have been morphinized, and many are children. Two grammes of Procaine, together with 0.5 gm. Pentothal and 1 gm. of Vitamin C, are added to the intravenous serum and the drip allowed to run at 60 to 80 drops per minute. After a few minutes the patient experiences relief of pain and the drip is slowed down to 40 per minute, this being increased if he complains of pain again. The burns are then cleaned and dressed and the drip is allowed to continue running at a slow rate (about 40 per minute). The patient will become drowsy and often go off to sleep. If the patient is very young (e.g. 4 years old), the Pentothal is reduced to 0.25 gm. and the Procaine to 1 gm. per litre.

We have used this combination to dress burns of all degrees. The following is an illustrative case:

Case 5. A young Bantu girl of 14 was admitted with extensive second degree burns of both arms and forearms, shoulders, neck, chest and back. She was in a very shocked condition, pulse 110 per minute, temperature subnormal, she was moaning with pain. The burns were about two hours old. An intravenous drip containing 2 gm. of Procaine Hydrochloride plus 0.5 gm. Pentothal in 1,000 c.c. of 5% dextrose in saline was commenced. The drip was run at 80 drops per minute. After about 10 minutes, the patient was able to sit up and have the burns dressed without suffering any pain. The dressings were completed in 25 minutes. The patient then went to sleep, pulse, 85 per minute, full and regular. The drip was now slowed to 40 drops per minute until the whole litre of fluid had been given. She was discharged nine days later.

(b) *For Post-Operative Pain.* Here we add 1-2 gm. of Procaine Hydrochloride to the post-operative drip, not using Pentothal. We feel that the patient has already had Pentothal during the general anaesthetic and that the addition of further Pentothal is neither warranted nor required. The drip is allowed to run at between 40 to 80 drops per minute, depending on the condition of the patient. Here again, if it is necessary to run the drip very slowly or very fast for any reason, the amount of Procaine is reduced or increased accordingly.

The relief of post-operative pain is usually marked and the amount of morphia needed post-operatively is cut down to a minimum. This relief of pain has been particularly noticeable in skin grafts where the donor area may cause post-operative pain. The following case is illustrative:

Case 6. A middle-aged Bantu man had a thoracoplasty performed for apical T.B. Four upper ribs were removed under Pentothal, d-tubo-curare, nitrous oxide and oxygen. The patient was awake on leaving the theatre, but very restless and distressed in spite of intravenous omnopon (¼ grain) being given to him. After about half an hour, the man was so restless that 1 gm. of Procaine was put into the blood drip, making a 0.2% solution. Ten minutes later the man was sleeping quietly.

5. FOR OBSTETRICS

Here a very small series of cases was done by one of us (Dr. Barlow) in conjunction with Dr. Hilde Ginsberg, some four years ago, using a 1% solution in a continuous drip. After four successful cases, the fifth case convulsed violently and we decided there were other forms of analgesia safer for the mother and child. We feel now that we might have had better

success if we had used the intermittent method advocated by Schmahmann (1950), but are unfortunately not in a position to do a series of cases at present.

6. FOR THERAPY

Our experiences in the field of therapy have been limited, and we have not to any great extent substantiated the glowing reports of the literature. One reason for this may be that the conditions treated in the Bantu have been of a chronic or long-standing nature in which irreversible changes have occurred, e.g. chronic rheumatoid arthritis. Our cases have included the following:

(a) *Toxic arthritis,* secondary to septic tonsils, in an Indian medical student. Here manipulation and treatment were greatly facilitated by the Procaine Hydrochloride, but as tonsillectomy was refused, the symptoms recurred.

(b) *Pruritus,* in a neurotic Coloured man. Here 150 mg. of Procaine Hydrochloride were given to the patient intravenously. The patient's itching disappeared and he appeared to be relieved, but on interrogation later, denied any relief lasting for longer than a quarter of an hour, and refused treatment by a continuous Procaine drip.

(c) *Cardiac arrhythmia.* In view of the spectacular results we have obtained in arrhythmias, when the patient was under general anaesthesia, our results here were particularly disappointing. Cases of auricular fibrillation and other arrhythmias failed to respond to intravenous Procaine. We have used up to 150 mg. in a 1% solution, but intend in future to increase the dose.

It is of interest to note Case 3 here. In this case, the intravenous Procaine stopped the arrhythmia whilst the patient was under general anaesthesia, but completely failed to do so when she was no longer anaesthetized.

(d) *To prolong the action of lumbar blocks*: Here 0.2% Procaine was given in a continuous drip after the lumbar block in order to prolong the effect of the block.

Many writers advocate Procaine Hydrochloride intravenously because of its vasodilation effect for ulcers, etc., of the lower extremities. As we have proved the efficacy of continuous caudals in these cases, we have not tried it here.

SUMMARY

The use of intravenous Procaine Hydrochloride is reported in a number of cases:

A suitable dosage, by the continous method, for analgesia and as an adjunct to anaesthesia is given.

The efficacy of Procaine Hydrochloride for burns and post-operative pain is emphasized.

Procaine Hydrochloride is advocated for controlling cardiac arrhythmias in chest surgery.

We have found Procaine Hydrochloride somewhat disappointing therapeutically, but further trial and a change of technique may be required.

The use of Procaine Hydrochloride as an anaesthetic does not appear to be substantiated, but as an analgesic or as an adjunct to anaesthesia, Procaine deserves a prominent place in anaesthesiology.

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VERENIGINGSNUUS : ASSOCIATION NEWS

BARAGWANATH MEDICAL SOCIETY: SEPTEMBER MEETING

Dr. Vernon Wilson presented two patients with advanced paralysis agitans and disturbance of respiratory function indicated by lowering of the femoral arterial oxygen saturation. Neither patient had had respiratory symptoms and there had been no evidence of bronchitis, emphysema, bronchiectasis, silicosis or any other respiratory disease, either in the history or during observation.

One of the patients, observed for six months, had been admitted on two occasions as a gross cor pulmonale with femoral arterial and venous oxygen saturation as low as 56% and 31% respectively.

Dr. Wilson showed X-rays of the chest which demonstrated, during the illness, a large heart shadow, prominent pulmonary arteries and widespread shadows throughout the lung fields and an absorption-collapse of the right lower lobe. This case had been followed in detail with serial blood oxygen saturation estimations and chest X-rays until the heart had returned to normal, the lung fields had cleared and the femoral arterial oxygen saturation had risen to 83% during convalescence. *Dr. Wilson* suggested that this disturbance could have been accounted for by diminished chest movement due to the spacticity of the respiratory muscles and he demonstrated how both the cases had very poor chest movement.

Dr. Wilson quoted the work of Motley, Cournand *et al.* who had shown that pulmonary arterial pressure rises in normal subjects when the respiratory tree is deprived of oxygen. He also reported that *Dr. J. C. Gilroy* and himself had demonstrated that by giving oxygen to an anoxaemic patient with cor pulmonale, the originally high pulmonary arterial pressure had been reduced to normal. In consequence, he believed that the poor respiratory movement in his patient with paralysis agitans had resulted in poor oxygenation and in turn pulmonary hypertension and cor pulmonale.

Dr. A. Watt said that he had not seen these patients develop cor pulmonale. The majority seem to die from pneumonia due to excessive salivation and a decreased cough reflex.

Mr. R A. Krynauw thought that *Dr. Wilson* had introduced a novel concept. It was possible that the anoxaemia in the cases discussed might bring about a metabolic upset and so be the cause of Parkinson's disease. He asked *Dr. Wilson* if in his experience he had seen any case of cor pulmonale developing Parkinson's disease. *Dr. Wilson* said he had not seen it before.

Dr. R Geerling discussed treatment in his experience of hundreds of cases. He found that Artane had doubtful results and seem to make the older patients much worse.

Dr. L. H. Horwitz presented for discussion the case of a Bantu male, aged 43 years, who complained of a pain in the neck for seven months. The pain radiated down the left arm to the dorsum of the hand. He also noticed a swelling in the neck for the same period of time. For the past four months his arms had become progressively weaker. Examination revealed a cachectic patient, holding his neck immobile. Enlarged matted glands were present on both sides of the neck. The tongue was wasted and more wrinkled on the left side and on protrusion, it deviated to the left. Fibrillation

was present. There was marked paresis in both arms, more so on the left. There was considerable wasting of the muscles of both arms, especially symmetrical wasting of the thenar eminences and to a lesser extent of the hypothenar eminences. There were no sensory changes in the arms or elsewhere. The abdominal reflexes were absent. The lower extremities were normal.

Special investigations showed a normal blood count and a doubtful blood Wassermann reaction. The pressure of the cerebrospinal fluid was 150 mm., the fluid was clear and there was no block. The fluid contained 3 lymphocytes, no polymorphs and no erythrocytes. The total protein was 162 mg. per 100 c.c., 79 mg. of sugar and 618 mg. of chlorides per 100 c.c. The Kolmer cardiolipin test yielded a doubtful result. A radiological examination of the heart showed it to be of normal size but there was a diffuse aneurysmal dilitation of the aorta. No abnormality could be detected in the radiological examination of the cervico-thoracic spine but a soft tissue swelling obscured the finer details. A gland biopsy revealed histological changes of tuberculosis. Three weeks after admission the patient developed a right-sided hemiplegia with a coarse nystagmus to the left and died four days later.

Mr. R. A. Krynauw was invited to discuss the differential diagnosis. He explained the different paths by which the tuberculous process in the neck could reach the cord.

He discussed in the differential diagnosis, amyotrophic lateral sclerosis, syphilitic amyotrophic lateral sclerosis and tuberculous pachymeningitis. He felt that in this case there was a local lesion at the level of the foramen magnum, the lesion lying in front of the cord, and pressing on the anterior spinal artery and affecting the anterior horn cells. The lesion was probably a tuberculoma acting by direct pressure or associated with endarteritis. An alternative diagnosis was a tuberculous pachymeningitis, but the spinal fluid was not in keeping with the latter.

Dr. I. Higginson. At autopsy the most striking feature was disruption of the lower portion of the medulla and upper part of the cord by pressure from the odontoid process of the axis. There was subluxation of the atlanto-axial joint due to tuberculous destruction of the transverse ligment of the atlas.

In addition there was an area of softening and necrosis in the left lobe of the cerebellum about 2 cm. in diameter. A small tuberculoma was also found in the pontine angle on this side.

No significant pathological lesion was observed in the midbrain or the cerebral hemispheres.

A NEW DIVISION

Northern Areas Division (C.W.B.)

The Northern Areas of the Cape Peninsula have grown considerably during recent years and there are now some 83 medical practitioners resident there.

The Cape Provincial Administration has promised that it will build a Hospital in the area in the near future, and has in the meantime established a Hospital Board.

Practitioners of the area, feeling the need for greater opportunity for meeting one another, decided to form a Division within the Cape Western Branch, and after preliminary discussions some 30 medical practitioners met at Parow on 4 October 1950. Dr. A. W. S. Sichel, President of the Association, and Dr. A. H. Tonkin, the Medical Secretary, were present, and both addressed the meeting.

It was unanimously resolved to form a new Division to be known as the Northern Areas Division of the Cape Western Branch, and Dr. H. W. Needham of Goodwood, was elected the first Chairman. Dr. J. R. E. Lee of Maitland, was elected Vice-Chairman, and Dr. M. Hoffman of Parow, agreed to be Honorary Secretary and Treasurer. The two Executive Committee Members elected were Dr. R. A. Webner of Bellville, and Dr. T. B. McMurray of Pinelands.

The constitution is to be drawn up and submitted at the next meeting.

Members are enthusiastic and look forward to meetings which will be helpful and interesting.

M. Hoffman,
Honorary Secretary.

Parow.
26 October 1950.

PASSING EVENTS

The American Society for the Study of Sterility: Annual Meeting—9 to 10 June 1951

The annual meeting of this Society will be held in Atlantic City, New Jersey, U.S.A., on 9 and 10 June 1951 and will conclude on the day before the opening of the American Medical Association Convention in the same city.

Overseas visitors who may wish to present papers should communicate with Dr. W. T. Pommerenke, Strong Memorial Hospital, Rochester, New York, U.S.A.

Empire Medical Advisory Bureau

South African medical practitioners who are thinking of visiting the United Kingdom should get in touch with Dr. H. A. Sandiford, Medical Director of the Bureau, at B.M.A. House, Tavistock Square, London, W.C.1, so that all the facilities of the Bureau will be placed at their disposal.

Medical practitioners will find the Bureau helpful in arranging accommodation as well as post-graduate courses of study.

* * * *

The American Dental Association has received a report that a tooth powder containing penicillin reduces the incidence of dental caries. The investigations were spread over five years at the Tufts College Dental School at Boston, Massachusetts.

The experimental animals were hamsters because they can be fed to develop dental cavities at the rate of nearly one a day. Control experiments with groups of elementary school children suggested that the penicillin tooth powder resulted in a 55% reduction in cavities.

It is claimed that there is evidence that this tooth powder (known as dentocillin) also slows tooth decay in adults.

* * * *

The recent United States National Conference on the Aging report that at the beginning of the present century one American in 25 was 65 years old or older. To-day the ratio is one out of every 13. This means that of a total population of 150 million, 11,514,000 citizens are 65 years old or older.

* * * *

Dr. R. Campbell Begg has returned to the Union after a short visit overseas.

* * * *

Dr. A. Wolpowitz, until recently on the staff of the X-ray Department of the General Hospital, Pretoria, has commenced private practice as a radiologist at Alphen Building, corner of Andries and Skinner Streets, Pretoria. Telephones:— Rooms: 2-4512; Residence: 2-8694.

* * * *

Dr. Cecil Moss and Miss J. Kalf were married in Durban on 15 November 1950.

* * * *

The United States Atomic Energy Commission reports that among the thousands of persons who worked with atomic energy during the last eight years in the United States, only two deaths and 13 injuries occurred. This is a remarkable tribute to the protective measures designed to guard workers and the public.

Births

To Dr. and Mrs. Jack Friedman, in Johannesburg, a son.

To Dr. and Mrs. C. C. Pretorius (*née* Tobie Muller) a daughter on 8 November 1950, at the Mowbray Maternity Hospital, C.P.

Opening of Allen & Hanburys (Africa) Limited New Laboratories

On Thursday, 12 October 1950, Mr. F. Capel Hanbury, Ph.C., J.P., Chairman of Allen & Hanburys Limited, London, opened the new laboratories of the African Subsidiary in Durban, in the presence of the Hon. D. G. Shepstone, Administrator of the Province of Natal.

There was a large gathering of doctors, pharmacists and leading industrialists at the official opening, after which a cocktail party was held at the Durban Country Club.

ADDRESSES UNKNOWN

The attention of the medical practitioners whose names appear in the list subjoined hereunder is invited to the fact that letters which were addressed to them by the South African Medical and Dental Council to their registered addresses have been returned by the Post Office undelivered. Their respective addresses appear in the records of the Council as indicated in the list. Registered letters have been sent to these practitioners in terms of Section 17 (i) (b) of the Medical, Dental and Pharmacy Act which reads as follows:—

17. (1) The council may erase from the register the name of any person who—

(b) has failed, within a period of three months from the date of an enquiry sent by the Registrar by registered letter to the address appearing on the register in respect of him, to notify to the Registrar his present address;

The practitioners concerned are requested to communicate with the Registrar, the South African Medical and Dental Council, P.O. Box 205, Pretoria, without delay in order to avoid the erasure of their names from the register.

Name	*Present Registered Address*
Dr. U. Birnbaum.	c/o Dr. J. Mibashan, 182 Main Road, Sea Point, Cape Town.
Dr. C. G. P. Bowker.	P.O. Winterton, Natal.
Dr. A. J. Brink.	13de Laan 118, Parkhurst, Johannesburg.
Dr. E. J. Doel.	P.O. Box 74, Broken Hill, N.R.
Dr. B. R. Fink.	Missionary Hospital, P.O. Box 15, Thaba 'Nchu.
Dr. H. A. C. Gregory.	31 Belvedere Avenue, Oranjezicht, Cape Town.
Dr. C. T. Jenkins.	P.O. Box 48, Amanzimtoti.
Dr. T. J. J. Jeppe.	Kimberley Hospital, Kimberley.
Dr. E. G. Lewis.	62 Millson House, Twist Street, Hospital Hill, Johannesburg.
Dr. G. W. Lund.	Umtata, Transkei.
Dr. J. L. K. Marais	70 Botha Avenue, Witbank.
Dr. F. A. F. MacKenzie.	R.M. Sick Bay, Simonstown, C.P.
Dr. V. Resnekov.	Department of Radiology, Groote Schuur Hospital, Cape Town.
Dr. V. Sarif.	52 Elray Street, Fairmount, Johannesburg.
Dr. J. H. S. van Reenen.	'Geluk', Philippolis, O.V.S.
Dr. F. Viedge,	57 Cumberland Street, Umtata.
Dr. J. W. Weston.	46 Kingslyn, St. Andrews Street, Durban.
Dr. E. Comay (Intern).	12 Kenwood Court, Claremont Avenue, Kenilworth, Cape Town.

REVIEWS OF BOOKS

LEUCOTOMY

Pre-Frontal Leucotomy. By Maurice Partridge, M.A., D.M. (Oxon.), D.P.M. (Eng.). (Pp. 496 + vi. 42s.) Oxford: Blackwell Scientific Publications Limited. 1950.

Contents: 1. Preface. 2. Introduction. 3. Scope of the Present Investigation. 4. Operative Technique. 5. Complications and Sequelae. 6. Preliminary Consideration of Changes at the Psychic Level. 7. The Post-Operative Personality as a Whole. 8. Cases with Affective Disorders. 9 Incontestably Schizophrenic Cases. 10. Schizophrenic Cases with Affective Colouring. 11. Cases with Recurrent Schizophrenic Illness. 12. Preserved Paranoid Schizophrenic Cases. 13. Other Schizophrenic Cases. 14. Obsessional Cases. 15. Psychopathic Personalities. 16. Cases of Drug Addiction. 17. Mentally Defective Group. 18. Cases with Disorders Associated with Organic Disease. 19. 'Parturient Montes'. 20. Bibliography. 21. Index.

This book appears at a time when the subject of leucotomy is much in the public eye and when there is a body of opinion that would rigidly control its practice. It is thus to us a timely publication; we but trust that those deputed to consider the matter in the best public interest will take the trouble to read the work very seriously. Mere scanning of such a book can do harm, especially in the impressionable mind of the 'good committee man', whose quick wit is all too often not balanced by sufficient attention to detail, whose decisions are too often forceful rather than mature, who too often and too readily creates a group of 'yes-men' on a commission.

Each and every member of a commission on the subject must conscientiously study this report. It is unbiassed, as the author had no part in the treatment of the cases, or in their selection. It studies the facts impartially, if indeed it is possible for any mind to be completely impartial! It presents the blackest side of the picture along with the brighter.

The methods used in this follow-up of 300 cases seem ideal in their simplicity and have many advantages over psychometric tests. People are studied as they are, in their normal surroundings, by a skilled psychiatrist, whose keen sense of humour alone seems to fit him excellently to his present role, over the shifting background of passing years; for surely disease, the effects of treatment, even life itself is kaleidoscopic and not static.

Through the whole work, through all its pathos, hope and humour, runs one constant plea. Post-operatively, in their escape from discipline, which may have been self-imposed, with their loss of driving force, with the blunting of the refinements of susceptibility, these patients are not among the great ones, the wise ones or the conquering ones of the earth; but their state must always be weighed against the pre-operative state and the prognosis in absence of operation.

At a time like this no medical man can afford not to read this book.

AIDS TO PSYCHIATRY

Aids to Psychiatry. By W. S. Dawson, M.A., D.M., F.R.C.P. (Lond.), F.R.A.C.P., D.P.M. (Pp. 329 + viii. Sixth edition. 6s.) London: Baillière, Tindall & Cox. 1950.

Contents: 1. Introduction. 2. Psychology. 3. Personality. 4. Psycho-Pathology. 5. Causation of Mental Disorders. 6. Classification of Mental Disorders. 7. Theories of the Psychoneuroses. 8. Neurasthenia and Nervous Exhaustion. 9. Anxiety States. 10. Hysteria. 11. Obsession. 12. Psychoneurosis in War. 13. Sexual Perversions and Anomalies of the Sexual Instinct. 14. Manic-Depressive Psychosis. 15. Schizophrenia. 16. Paranoid States. 17. Toxic Psychoses. 18. Alcoholism. 19. General Paralysis. 20. Epilepsy. 21. Dementia. 22. Mental Disorders associated with Physical Diseases. 23. Differential Diagnosis of Certain Mental States. 24. Mental Deficiency (Amentia) (Oligophrenia). 25. Child Psychiatry. 26. Treatment. 27. Legal Aspects of Insanity. 28. Psychiatric Examination. 29. Mental Hygiene. Index.

This member of the *Aids* series, now extensively revised, will provide all interested in psychiatry with a full account of the subject. The abundant information packed in this little book will aid not only those preparing for examination in psychiatry but also those in practice.

CELL PHYSIOLOGY AND PHARMACOLOGY

Cell Physiology and Pharmacology. By J. F. Danielli, Ph.D., D.Sc. (Pp. 156. 24s.) London: Cleaver-Hume Press Ltd. 1950.

Contents: 1. The Cell as a Physio-Chemical Unit. 2. Possible Actions of Drugs on Surfaces. 3. Membrane Permeability and Drug Action. 4 Enzymes and Drug Action. 5. The Actions of Narcotics. 6. Responses of Cells on the Biological Level.

This book is based on lectures given by Professor Danielli at University College, London, to indicate some of the more important factors concerning drug action on cells. Study of cell morphology is obviously not enough. Every cell must be considered as an organized system of activity. The manner in which drugs exert their action on cells is one of the fundamental problems of physiology.

Pharmacologists, chemists, biologists and doctors will find this book valuable in showing the problems encountered in searching for new drugs and in investigating drug action. According to the author, who has had practical experience in these problems, the chemical aspects are reasonably easy and precise. Paucity of information on the biological side leads to theorizing by the chemist, with much waste of time in the synthesis of useless compounds, and in their testing by biologists. This book aims to stimulate biological research on drug action.

The author discusses clearly and concisely the cyto-chemical and physico-chemical aspects of the cell, the cytoplasm, chromosome and gene structure. He then considers the interactions of ions at surfaces and the actions of drugs at surfaces. Next is presented the penetration of drugs through cell membrane and the permeation through other complex

membranes. Subject to reservations the permeability of a cell to a drug can to some extent be calculated. These permeability problems are of practical importance in regard to the access of drugs to organs, and the information may aid the design and testing of new drugs.

The interesting work of recent years on the action of drugs on cellular enzymes is next considered with the conclusion that drugs often act on enzyme systems, but rarely act on enzymes only. The various theories of narcotic action are considered in detail; whether the action is on the cell surface, due to partition of the narcotic between an aqueous phase and lipoid phase, or mediated primarily through enzyme systems.

In the final chapter a number of types of biological response is examined, including the effects of mitotic poisons (important in the chemotherapy of cancer), and the responses of genetic systems to drugs.

TEXTBOOK OF RADIOTHERAPY

A Short Textbook of Radiotherapy for Technicians and Students with a Supplementary Chapter for the Dermatologist. By J. Walter, M.A., B.M. (Oxford), M.R.C.P. (Lond.), D.M.R.E. (Camb.), and H. Miller, M.A., Ph.D. (Camb.), F. Inst. P. Foreword by J. L. A. Grout, M.C., F.R.C.S. (Ed.), F.F.R., D.M.R.E. (Pp. 444 + xii. With 199 illustrations. 28s.) London: J. & A. Churchill Limited.

Contents: 1. The Structure of Matter. 2. The Physical Properties of X-rays. 3. The Generation of X-rays for Therapy. 4. The Physical Aspects of X-ray Therapy. 5. Physical Properties of Radioactive Materials. 6. Biological and Pathological Introduction. 7. Biological Effects of Radiation. 8. Methods of Radiation—Radium. 9. Methods of Radiation —X-rays. 10. Principles of Treatment and Dosage. 11. Illustrations of Technique in Malignant Cases. 12. Illustrations of Technique in Non-Malignant Cases. 13. The Protection of Staff in Radiotherapy Departments. 14. Duties and Responsibilities. 15. (Supplementary Chapter). Radiotherapy in Dermatology. Appendix. 1. Recommendations of the British X-ray and Radium Protection Committee. 2. Artificial Radioactivity and its Medical Applications. Book List. Addendum. Index.

Until the publication of this book there had not been a textbook of radiotherapy specifically written for the student preparing for the Diploma of Radiography. For this reason, this book fulfils a long-felt want.

In the reviewer's opinion it can well be recommended to a much wider circle of readers than those preparing to become radiographers. It serves as a very satisfactory introduction to a subject in which the medical student rarely receives sufficient instruction.

For the student intending to take the Diploma in Radiotherapy the syllabus has been completely surveyed. The physics of radiation, both of X-rays and radium, has been lucidly discussed in a concise manner. The methods of application of the various types of X-rays and radium have been preceded by descriptions of the biological effects of these radiations.

The technique employed in the treatment of the commoner malignant and non-malignant lesions is clearly described and liberally illustrated with photographs and diagrams. The way in which a course of therapy is planned and the application of the prescription is well defined.

The reviewer has no hesitation in recommending this as a standard textbook to the student; the qualified radiographer could well use it as a reference book.

GASTROENTEROLOGY

Postgraduate Gastroenterology. Edited by Henry L. Bockus, M.D. (Pp. 670 with 258 figures. 85s. or $10.00.) Philadelphia: W. B. Saunders Company. 1950.

Contents: 1. The Esophagus. 2. Gastric Secretion. 3. Gastric Neoplasms. 4. Peptic Ulcer. 5. Application of Neuropsychiatry to Gastrointestinal Problems. 6. Symposium on Secondary Gastrointestinal Disorders. 7. Symposium on the Pancreas. 8. Symposium on Abdominal Pain. 9. Presentation of Cases. 10. The Liver. 11. Presentation of Cases. 12. Chronic Non-Specific Enteritis and Entero-Colitis. 13. Intestinal Obstruction. 14. Current Problems of Diagnosis and Therapy. 15. Chronic Ulcerative Colitis. 16. Carcinoma of the Colon. 17. Presentation of Cases. Index.

This book was sponsored by the teaching and research staff of the Graduate School and Medical School of Medicine of the University of Pennsylvania, and is a written record of the proceedings of a course in Gastroenterology given in December 1948, under the aegis of the American College of Physicians. The Editor is Dr. Henry Bockus, so well known to gastroenterologists and the contributors are drawn from some of the best known of the Medical Schools and Research Institutions of America. The proceedings of a relatively small group of specialists is recorded in a volume of some 600 pages, printed on art paper and containing excellent reproductions and artistically drawn illustrations, and is a proof of the magnitude of the resources in money and personnel that can be mobilized in medical circles in the United States of America.

No attempt has been made to make this a complete treatise on gastroenterology. The volume prints papers that were read during some 13 symposia on recent advances in certain aspects of gastro-intestinal disease, together with case presentations, and a verbatim report of the discussions that followed, so that the reader is given a critical view of the pros and cons of some of the unsettled problems presented at the congress.

Of the dozen sections in the volume, those on the oesophagus, the physiology and clinical aspects of the vagotomy problem, gastric secretion, and ulcerative colitis are outstanding. An account of lysozyme (mucolytic enzyme) activity in ulcerative colitis and a preliminary report on antilysozyme therapy is of much interest.

This publication will be much appreciated by gastroenterologists for the authoritative account it gives of recent advances in the subject and all physicians will find in it much to stimulate them.

DISEASES OF LABORATORY ANIMALS

Notes on Communicable Diseases of Laboratory Animals. By H. J. Parish, M.D., F.R.C.P.E., D.P.H. (Pp. 69. 3s.) Edinburgh: E. & S. Livingstone Ltd. 1950.

Contents: 1. Guinea-Pigs. 2. Rabbits. 3. Mice. 4. Rats. 5. Hamsters. 6. Ferrets. 7. Monkeys. 8. Cats. 9. Dogs. 10. Pigeons. 11. Canaries. 12. References.

This booklet is intended to be a convenient reference book for those interested in the maintenance of a healthy stock of laboratory animals. It is an all too common experience that the diagnosis of spontaneous disease in laboratory animals is neglected because of the inconvenience of obtaining information from existing and more elaborate books on laboratory animal diseases. Without an adequate diagnosis effective control measures are often neglected.

The conciseness of this book will encourage its use. It is, however, unfortunate that the author has not made it more readable by avoiding the somewhat telegraphic style in which it is written.

HUMAN MILK IN WARTIME

Human Milk: Wartime Studies of Certain Vitamins and Other Constituents. By S. K. Kon and E. H. Mawson. (Pp. 188. 4s.) London: H.M. Stationery Office. 1950.

Contents: 1. Introduction. 2. The Constituents of Milk: A. The Fat Content of Milk. B. The Solids-not-fat and its Constituents. C. The Biological Value of the Proteins of Milk. D. The Vitamin A and Carotenoid Content of Milk. E. The Vitamin D Content of Milk. F. The Vitamin B_2 Content of Milk. G. The Riboflavin Content of Milk. H. The Vitamin C Content of Milk. 3. The Relationship between the Constituents studied and Nutritional Standards: I. A Study of the Composition of Milk throughout an Individual Lactation of 33 Weeks. J. Dietary Studies with Lactating Women at Shoreditch. K. A Comparison of the Composition of Milk at Glasgow and Shoreditch. L. The Composition of Milk in Relation to the Nutritional Requirements of Mother and Child. 4. Summary and Conclusions.

This report is based on an extensive investigation at the National Institute for Research in Dairying during the War years 1941-1945. The investigation involved the organization of three large dietary surveys and the collection and analysis of single specimens of milk from more than 2,000 nursing mothers. It was hoped to show in what degree inadequacies in the British national diet might be reflected in the composition of breast milk, and to use the constituents of her milk as a measure of the mother's nutrition. The constituents studied included vitamin A, carotenoids, vitamin B, riboflavin, ascorbic acid, fat, solids-not-fat, lactose, total nitrogen, calcium, phosphorus and vitamin D.

It was realized that factors besides the dietary intake of

the mother affect the composition of her breast milk. As such, the influence on lactation of the time of day, stage of feeding, milk yield, the age of the mother and her parity were carefully investigated.

Many important observations have been revealed, particularly with regard to the vitamin content of human milk. In this connexion one may note the rise of vitamin B content of milk following the introduction of national wheatmeal bread. A similar rise of vitamin C content followed closely on the arrival and distribution in Britain of a large consignment of citrus fruits. In view of the constant drain of vitamins from the mother's system during lactation, the necessity for an adequate amount in the maternal diet is stressed.

The material provided by this comprehensive survey is an invaluable addition to present knowledge on the subject, and one must congratulate Dr. Kon, Mrs. Mawson and their numerous co-workers on this fine work.

THE TRIAL OF DR. BUCK RUXTON

Trial of Buck Ruxton. Edited by R. H. Blundell and G. H. Wilson, M.D. (Pp. 457 + lxxxvii, with 20 illustrations. Second edition. 15s.) London, Edinburgh, Glasgow: William Hodge and Company Limited, 1950.

Contents: 1. Introduction. 2. Table of Dates. 3. The Trial. 4. First Day, Monday, 2nd March 1936. 5. Second Day, Tuesday, 3rd March 1936. 6. Third Day, Wednesday, 4th March 1936. 7. Fourth Day, Thursday, 5th March 1936. 8. Fifth Day, Friday, 6th March 1936. 9 Sixth Day, Saturday, 7th March 1936. 10. Seventh Day, Monday, 9th March 1936. 11. Eighth Day, Tuesday, 10th March 1936. 12. Ninth Day, Wednesday, 11th March 1936. 13. Tenth Day, Thursday, 12th March 1936. 14. Eleventh Day, Friday, 13th March 1936. Appendices.

This is the completely definitive account of a very remarkable murder. Dr. Buck Ruxton, a Parsee doctor practising in England, was found guilty of the murder of his wife. The evidence strongly suggests that he also murdered the servant girl of the household, because she witnessed the first killing.

The non-medical aspects of this case history have a great interest in their own right; but they cannot compare, in this respect, with the extraordinary achievements of anatomical reconstruction responsible for establishing the identity of deceased persons, who were so skilfully dismembered by the murderer as to suggest a sound knowledge of surgery.

The verbatim record of the trial includes in appendices the detailed medical reports of the two main investigators as well as radiological and other reports prepared by other experts involved in the amazingly accurate reconstruction.

The labours of Prof. John Glaister of Glasgow and Prof. James C. Brash of Edinburgh were indeed prodigious, and in many respects their evidence constitutes models to be followed. At no time were these witnesses prepared to stretch the reasonable scientific inferences which could be drawn from their data, so as specially to fit the Crown hypothesis. Whenever they could make a point in favour of the accused person, they did not hesitate to do so.

Professor Glaister's evidence about how the presence of soap might interfere with the precipitin test for human blood becomes a valuable statement of the position which should guide medico-legal pathologists in all parts of the world; not only on the technical points involved, but also in respect of the honest doubts which an expert witness may entertain and should never hesitate to express.

The technique of photographing a skull and superimposing it, natural size, on photographs of the deceased persons taken during their lifetime, is a completely novel one in forensic research and was probably used for the first time in this case. Although proof of identity based on such data cannot ever be completely conclusive from the lawyer's standpoint, Professor Brash's achievements in this particular field represent a very impressive contribution which will evoke respectful attention from all those who study this trial.

This record of the trial also makes available the authoritative opinions of the expert witnesses on the finding of the cyclopean eye which was mixed up with the human remains.

In spite of the nature and the general excellence of the evidence of the medical witnesses, it remains extraordinary to read Professor Glaister's views on the subject of the liquidity of the blood in cases of death from asphyxia. He makes the statement (p. 157) that in 'asphyxial death there is an increased interval of time during which fluidity of blood may remain—up to 12 hours or thereabouts, but I would not be certain'. From the manner in which Counsel put the question to Professor Glaister it seemed that he might challenge this view. It is strange, therefore, that Counsel did not pursue this point in cross-examination, because there is no scientific evidence to support Professor Glaister's opinion and there is considerable scientific evidence to controvert it.

In a recent review of the problem Mole (J. Path. Bact., 1948, 60, 413) states: 'Emphasis on the fluidity of the blood as characteristic of any special cause or mechanism of death is probably misplaced . . .'. This is in keeping with observations reported by Yudin (The *Lancet*, 14 August 1937) in his work on cadaver blood and confirms what Hunter wrote as long ago as 1794: 'In many modes of destroying life the blood is deprived of its power of coagulation, as happens in sudden death produced by many kinds of fits, by anger, electricity or lightning; or by a blow on the stomach, etc. In these cases we find the blood, after death, not only in as fluid a state as in the living vessels, but it does not even coagulate when taken out of them'. This incoagulability of the blood is a commonplace at autopsy and the finding of clots is the unusual thing.

Mole came to the conclusion that the liquidity of the blood was a feature of 'sudden' death associated with 'shock or collapse' during life. The mechanism appears to be the production of a fibrinolysin which may fail to develop in certain deaths associated with infection and cachexia, thus explaining the presence of abundant clot in the heart as well as in the limb vessels in such cases.

Mole also makes the important observation that 'fluid and coagulable blood was always found whatever the cause of death when the autopsy was carried out within an hour or so of death'. It is clear that in cases of 'sudden' death the blood remains spontaneously coagulable 'only during a brief period after death and then becomes completely free from fibrinogen' (Mole, *ibid.*, p. 419).

Where the matter has been put to the experimental test in animals, Professor Glaister's view has also been found wanting. Ponka and Lam (Proc. Soc. Exp. Biol. Med., 1948, p. 334) concluded that severe asphyxia, experimentally induced, did not have any effect on the clotting properties of the blood of dogs.

It looks as if many medico-legal pathologists have mistakenly come to associate the common occurrence of liquid and incoagulable blood found at autopsy in a great variety of different kinds of death as a diagnostic sign of the anoxic type of death occurring in asphyxia. This completely disregards the properties of cadaver blood, which are in great measure determined by the post-mortem interval. This erroneous view has been perpetuated from textbook to textbook, and the time for its correction is certainly overdue.

It is, of course, not suggested that Glaister's views on the coagulability of the blood in death from asphyxia would have altered the findings of the Court. It is, indeed, certain that they would not have done so. The matter has been referred to because it is the only weak spot in what was undoubtedly a most outstanding and memorable expert medico-legal performance. It certainly does not detract from the value of Professor Glaister's evidence in general. In fact, it adds considerably to the interest with which the medical reader will approach this comprehensive record of one of the most remarkable murders of all times.

THE RHESUS DANGER

The Rhesus Danger: Its Medical, Moral and Legal Aspects. By R. N. C. McCurdy, M.B., Ch.B., D.P.H. (Pp. 138. 5s.) London: William Heinemann, Medical Books Limited. 1950.

Contents: 1. The Rhesus Problem: The Medical Background. 2. The Rhesus Problem: Some Wider Issues.

Dr. McCurdy has prepared a very comprehensive account of many aspects of the Rhesus problem not commonly dealt with in expositions of the Rh factor, its genetics and its serology.

These latter aspects are also most succinctly set out; but the added value of this booklet is the useful survey of the literature on wider issues which are involved in a study of the Rhesus problem. The thoroughness of the survey is reflected, e.g. in the chapter on Abortion in which the author quotes the opinion of Masters on the legal position in South Africa.

Dr. McCurdy's volume is a minor encyclopaedia on the implications of Rh, written in a manner most excellently suited to the general practitioner as well as the intelligent layman interested in this vital problem.

CORRESPONDENCE

GROOTE SCHUUR HOSPITAL: DISPENSING SERVICES

To the Editor: *Consultant Physician*, in his letter of 21 October, draws attention to the deplorable state of affairs existing at the Out-Patient's Department at Groote Schuur Hospital.

He considers that members of the Honorary Staff are virtually being compelled to perform a modified type of euthanasia by sending patients home to die, patients who have a good chance of survival if admitted to the hospital for treatment.

This is bad enough but it is not the worst.

Physicians consult in the mornings and they do not know what happens at 'closing-down time' in the afternoons at the Paediatric Clinics.

On numerous occasions during the past few months consulting paediatricians have been confronted by a dozen or so of distressed mothers with their sick children who have been turned away from the dispensary at 5 p.m. after waiting in queues for hours.

Many of these children are seriously ill and should have been admitted to hospital, but have to be sent home on account of the lack of accommodation. However, this makes no difference. At the appointed hour the dispensary windows are closed in their faces and they are unable to procure the prescribed medicines which are so often urgently required.

Now, Sir, we cannot always admit patients on account of the lack of accommodation and we sometimes have to keep them waiting for hours. It is inexcusable, however, to allow them to proceed home at the end of their weary day without being given the remedies which would give them some chance to carry out domiciliary treatment.

In spite of the appeals of members of the Honorary Staff, who have been prepared to work until the last patient has been attended to, nothing has been done. As a matter of fact, the situation has deteriorated and a notice was circularized this week to the effect that the dispensary will close at 4 p.m. owing to shortage of staff. It should be noted in this connexion that members of the medical staff have no access to the dispensary, else they would never allow their patients to proceed home without the medicines which they require urgently.

Consultant Physician has done a service to the public in bringing this matter to the notice of the medical press. Let the Provincial Administration realize that this is by no means a lonely voice in the wilderness, but that the patience and the tolerance of the medical profession have reached breaking point.

Free hospitalization for the general public is a farce as long as there are not sufficient beds available for the indigent sick. Cutting budgets is foolish if there are not even sufficient funds to ensure reasonable dispensing services.

A big teaching institution like the Groote Schuur Hospital should be an example of efficiency to the smaller hospitals, municipal welfare centres, Government Health Centres and general practitioners. But what an example we set—sending seriously ill people home to die without any attempt being made at treatment and that for no other reason but the lack of dispensing services.

Consultant Paediatrician.

Cape Town.
7 November 1950.

APPETITE IN ROSEOLA INFANTUM

To the Editor: In an article on roseola infantum which appeared in the *Journal* on 7 October 1950, Dr. Eric Kahn states that a preservation of appetite is one of the cardinal symptoms of the disease. In my report [1] of 16 cases, five ate normally but in 11 the mothers observed some loss in appetite. Anorexia was used as a general term to cover a mild, moderate or severe loss of appetite. There is not necessarily a complete loss, many of the infants partaking of less food than usual or eating well on one day but poorly on the next.

Many authors have recorded their observations on the appetite in this disease. Moore [2] stated that there may be anorexia; Rudolph [3] mentioned nausea and Greenthal [4] recorded that the infant 'refuses most of his food'. Zahorsky [5] says that 'anorexia may continue for two to five days'. On the other hand Clemens [6] in reviewing 80 cases did not mention the appetite specifically and Barenburg [7] stated that the children were comfortable, rested well and took nourishment.

Apparently, then, the appetite varies in this disease as do so many of the symptoms. Cases will be missed if the disease is ruled out in the presence of a loss of appetite.

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F. Walt.

125 Trust Buildings,
Gardiner Street,
Durban.
23 October 1950.

PRIMARY CARCINOMA OF THE LIVER AND INCLUSION BODIES

To the Editor: In a most interesting paper in this *Journal* (14 October 1950) Dr. W. O. Fischer states that he has observed inclusion bodies resembling rickettsia in the pituitaries of 17 non-Europeans who died as a result of primary carcinoma of the liver. These observations and subsequent investigation have made him think along the following lines:—

1. That the inclusion bodies may be a factor in the causation of carcinoma of the liver.
2. 'The presence of such bodies in the hypophysis of these cases may be merely accidental'.

I believe that there are two additional possibilities that cannot yet be excluded:—

1. That the conditions which caused the carcinoma may be the cause, or may be factors in the causation of the inclusion bodies;
2. That the inclusion bodies may be the *effect* of the neoplasm, e.g. superimposed infection of the neoplasm.

S. Sament.

122 Jules Street,
Belgravia,
Johannesburg.
26 October 1950.

TREATMENT OF CHICKENPOX AND SANDWORM INFECTION

To the Editor: Opportunities for research in general practice are frequent but the necessary time and library facilities for proper reporting are not always available. It is these considerations which constrain me to request the courtesy of your Correspondence Columns to bring to general notice two new treatments for common conditions which deserve wider trial.

Herpes Zoster and Chickenpox. Having noticed that T.E.A.B. and related compounds were being used for the relief of post-herpetic pain, I decided to try it with a view to avoiding the pain altogether. I had two cases (Native) of 24 hours' standing; they received 5 c.c. 10% T.E.A.B. (Boots) and within three days the lesions were quite dry; within five days they were completely healed. Following the injection there was no itching and no pain.

In view of the accepted relationship between herpes and chickenpox, I took the opportunity of a mild epidemic to try the same treatment. Thirteen cases were injected with doses varying from 2 c.c. to 5 c.c. according to age. In all but one case itching stopped almost immediately, the spots were dry in three days and gone in one week. The remaining case had two spots which had become septic before the treatment was started and these persisted somewhat longer. One child, a

daughter of the last case, was not treated as the infection seemed very mild. The spots followed the normal course, errupting for 7-8 days and remaining for three weeks.

Presumably when the erruption has disappeared the danger of infection is also over. It may be that this treatment will enable the quarantine period to be cut from the usual four weeks and thus save considerable loss of school-time.

Sandworm Infection. This condition is very rife in Zululand and the number of remedies almost equal to the number of cases. On a suggestion from Dr. Colin Black of Durban I tried the effect of an acetarsol (Orarsan, Boots).

Thirty-one cases have so far been treated, with complete success in four days or less in 27. The other four cases were either multiple or grossly septic. These responded to a further course preceded by Penicillin.

The basic course was gr. 4, t.i.d. for four days. Experience seems to indicate that adjustment of dose to body weight may improve the results and that the removal of any obvious sepsis first, is essential.

With the opening of the new 'sandworm season', this modification will be tried.

I shall be very pleased to give any further information to anyone interested and also to receive reports of other trials.

P.O. Box 24 Philip H. Dalgleish
Kwambonambi
Zululand
2 November 1950

GENERAL PRACTICE

To the Editor: The following remarks have been stimulated by Prof. J. F. Brock's and Dr. D. R. Meiring's articles published in the *Journal* of 21 October 1950.

Professor Brock deplores 'the dwindling contact with the family as a unit' in general practice, and 'the deterioration of the old-fashioned doctor-patient relationship', in which '. . . the decisive part has been played by the rapid expansion of medical diagnostic and therapeutic knowledge, which have placed a premium upon the specialist'.

Sir Francis Frazer, in an address to the Royal Medical Society in Edinburgh, on *Medicine in the New Social Order*, (*Lancet*, 1949, **1**, 132) states that 'the challenge (to medicine) is above all to the family doctor and the general practitioner'. If the general practitioner or family doctor is to avoid extinction, he must take up this challenge. He must develop new techniques of practice which will demonstrate that general practice requires specialized training, in much the same way as do other specialties. If he fails to produce the techniques which family practice demand, he will become as out-moded in the practice of medicine as the horse and buggy are out-moded in the sphere of modern transport.

Deterioration in his status and in the doctor-patient relationship are directly proportional to the lack of advance in techniques of general practice, and inversely proportional to the scientific and technological advance which has heralded the Specialist Register. Despite the fact that he has not been trained for general practice by his medical school, the general practitioner can maintain his status, and the cherished doctor-patient relationship, if he develops techniques of practice, as up-to-date (if not so dramatic) as cardiac catheterization in the specialty of Cardiology.

I should like to mention a few modifications of traditional general practice, which are being tried out. Although none of them is original, they might be added to the list of suggestions for the rehabilitation of general practitioners, offered by Dr. Meiring in this *Journal* (21 October 1950).

1. *Limitation of the Number of Patients.*
   (a) By defining the area in which a practitioner works; or
   (b) By restricting the number of families under his care.

This technique has been advocated, and translated into practice, for rural native practice, and is being elaborated for urban and semi-urban Native, Coloured, Indian and, with modifications, European communities (S. L. Kark (1944): S. Af. Med. J. **18**, 100; S. L. Kark and E. Kark (1945): Clin. Proc., **4**, 285.)

The National Health Service of Britain has also applied a restriction to the number of patients per doctor, between 2,000 and 4,000. (N.H.S. Act 1946.)

2. *Utilization of Trained Ancillary Personnel.*
   (a) Nurses.
   (b) Laboratory Technicians.

Pinsent, writing on the *Future of General Practice* (Lancet, 1950, **1**, 917) makes recommendations for a 'general-practitioner nurse' to assist the general practitioner. Unfortunately, hospital training alone does not equip the average nurse for general family nursing practice. A 'Family Nurse' is being trained at the Training Scheme for Health Personnel, Durban, to assist the Medical Officer in Health Centre practice (S. L. Kark, (1950): S. Af. Nursing J.; H. Cohn, (1950): Brit. J. Health Educ.)

Of the 'general-practitioner nurse', Pinsent writes: 'her value would be greatest in the home, where need for education of the patient is greatest. In time, perhaps, patients would recognize her as the first person to consult on minor ailments.'

As regards laboratory services, there is little doubt about the value of blood, sputum, stool, urine, smear, etc., investigations in every-day diagnosis and treatment. Pinsent would add radiographers to the personnel whose services would be available to the general practitioner.

3. *Preventive and Promotive Work.*

Professor Brock (S. Af. Med. J., 21 October, 1950) maintains that 'if doctors showed themselves to be proficient in the prevention of disease and the promotion of health, people would be only too willing to pay fees for these services'. The following modest beginning in preventive practice is suggested:—

(a) Immunization of all the members of the families (and their servants) under the practitioner's care; or instruction in the making use of existing Public Health or Local Authority facilities.

(b) An Ante-natal Care Programme. The Family and Home Nurse is a help here; (F. C. Naish, (1950): *Lancet*, **2**, 414.)

(c) A Mother and Infant Care Programme. The Family and Home Nurse is a godsend here (Alan Moncrieff, (1950): Brit. Med. J., **2**, 798.)

(d) A periodic medical examination of every member of the family. The results of such examinations should provide enough material to make use of the specialist in his rightful capacity, viz. consultant without the patient necessarily being admitted to hospital.

(e) Community health education work should temporarily be left to personnel qualified to do it, until such time as the practitioner is trained (or trains himself) in these methods of promoting health.

Such personnel are known as Health Educators in the U.S.A., and in the Health Centre Service of the Union Health Department, Health Assistants are trained as Health Educators. As specialists in promotive health work, part of their job is to instruct people in how to care for their own health by availing themselves of existing facilities, i.e. by helping themselves rather than relying on chemists, quacks and 'old wive's tales'.

This modest start points towards a re-orientation in family doctoring, not a return to the 'good old days'. It points towards group practice, but the 'group' must obviously include ancillary personnel (*National Health Services Commission Report*, 1944). At present training along these positive lines of family practice is only post-graduate, e.g. Training Scheme for Health Personnel. If the re-orientation were brought about in undergraduate training, it would accelerate the rehabilitation of family practice and the family doctor. This calls for a revision of undergraduate medical teaching.

I do not presume to deal with the subject of Medical School curricula in one paragraph, but take this opportunity of pointing out obvious reforms:—

(a) Physiology should be extended beyond the experimental animal and the laboratory to cover the whole man (including his psyche), the phases of his development, his family, and the society of which they are part (Dicks, H. V. (1950): *Lancet*, **2**, 317.)

(b) Pathology should be expanded beyond the morbid study of man's systems, to the whole man, the family and society.

(c) The pursuit of one or both of these will take undergraduate teaching out of the laboratory and hospital, into the consulting room and the home. The unit of study for the family doctor is no longer the cell, but the whole man, and perhaps, preferably, even the family *per se*.

In this note, the question of remuneration has been deliberately omitted, as being secondary to my purpose.

P.O. Box 27 J. S. Davidson, M.B., Ch.B.
Kloof
Natal
3 November 1950

DERMATOLOGISTS AND RADIO-THERAPY

To the Editor: Owing to my absence overseas I could not answer Dr. Gordon's letter (S. Af. Med. J., 22 July 1950, **24,** 612) before.

I made enquiries in numerous hospitals in England, and in Sweden, and dermatologists and others may be interested in the following observations:—

1. I could not discover any University or other institution which gives a diploma in dermatology. Although a dermatologist has to produce a certificate to the Medical Council that he has done post-graduate training in dermatology, he does not have to produce any certificate that he is competent to give X-ray treatment.

Dr. Gordon in his letter states: 'I cannot see any reputable institution issuing such a qualification, or certifying any such training without being satified that the candidate is competent to carry out such X-ray therapy'.

I could not discover any institution which gives any certificate, in Great Britain or in Sweden, of competence as far as X-ray therapy is concerned.

The Secretary of the Institute of Dermatology in London informed me that he knew of no institution which gives such a certificate, and the Institute of Dermatology does not give any such certificate. Perhaps Dr. Gordon will inform us which institutions give such certificates in relation to X-ray therapy.

I could not discover any institution which gave organized practical instruction in the use of X-ray therapy. Professor MacWhirter gives some lectures on the biologic effects of X-rays and radium at Edinburgh, but no practical instruction is given.

2. The knowledge of the indications and contra-indications of radiation therapy in dermatology no more indicates that a dermatologist is qualified to give radiation therapy than a knowledge on the part of an ear, nose and throat surgeon, or chest surgeon, of the value of radiation in their spheres, qualifies them to give such treatment.

3. Dr. Gordon makes a great point that *Mc.Kee and Cipollaro*, dermatologists, have written a book on the subject of X-ray therapy, and concludes from that, that X-ray therapy is an integral part of the dermatologist's technique.

4. Sir Stanford Cade has written a most outstanding book on radium therapy. Does that indicate that every surgeon can do his own radium therapy?

5. Dr. Gordon regards my strictures on the treatment of neoplasms by dermatologists as 'unreasonable'. My views on this subject are supported not only by leading radio-therapists, but also by dermatologists.

6. I inquired at the following hospitals in London:

The Middlesex Hospital.
The Royal Northern Hospital.
The Prince of Wales Hospital.
St. Bartholomew's.
Guy's.

In none of these hospitals is the dermatologist allowed to treat a malignant skin condition, whether it is a rodent ulcer or any other type of malignancy.

Dr. Barber, at Guy's, a leading British dermatologist for the last 30 years, authorized me to state that although he considered that dermatologists could treat non-malignant conditions, he himself invariably sent all malignant skin conditions to the radio-therapist.

I did not hear of any London hospital where the dermatologists did treat malignant skin conditions.

7. I made enquiries in Manchester. At the Salford Skin Hospital, dermatologists may prescribe doses up to 150 r per week, for a limited number of weeks. A radio-therapist attends from the Holt Radium Institute, supervises the X-ray therapy and prescribes treatment for the malignant conditions. The dermatologist does not prescribe treatment for malignant conditions.

8. At Liverpool, dermatologists are not allowed to treat malignant conditions or any condition requiring radiation up to critical dosage.

9. At Edinburgh Professor MacWhirter of the radio-therapy department at the Royal Infirmary, by arrangement with the Professor of Dermatology, Dr. Percival, treats all malignant skin conditions, and although the dermatological department has an X-ray machine, the dermatologists only prescribe doses up to a total of 450 r at 80 K.V. through 1 mm. aluminium. The radio-therapist is then consulted. The radium has been taken away from the dermatological department.

10. At Cambridge, malignant conditions of the skin are treated by radio-therapists, and not by dermatologists.

11. Dr. F. Bray, of the Sydney Hospital, Australia, informed me that the dermatologists prescribe the doses for benign conditions. The radiologist supervises this dosage. Malignant conditions are seen by the dermatologist with the radiologist.

12. Dr. Cooper, of Brisbane, Australia, told me that the dermatologist is not permitted to treat malignant skin conditions. He is only allowed to prescribe up to 500 r for non-malignant conditions.

13. In Stockholm (and this applies throughout Sweden) the dermatologists are not allowed to do any X-ray treatment at all. Professor Berven, of the Radiumhemmet, told me of a dermatologist, who had spent two years at the Radiumhemmet and who subsequently wanted to do his own X-ray therapy, in a large new municipal hospital (The Southern Hospital), but was not permitted to do so by the committee of the hospital, which insisted on the patients going to the X-ray department.

14. It should be noted, too, that anybody who wants to use an X-ray machine in Sweden, must obtain a licence from the Institute of Biophysics in Stockholm, and this institute does not grant certificates readily.

15. Dr. Gordon also appears to have overlooked that Dr. Leeming, who started this correspondence, agreed that dermatologists should not treat malignant disease.

16. It would appear then as far as Australia and Great Britain are concerned, although some institutions permit dermatologists to treat benign conditions, under the supervision of the radio-therapist, up to a certain level of dosage, which is regarded by the radio-therapist as safe, at no institution, in Australia, Great Britain or Sweden, is the dermatologist permitted to treat malignant conditions of the skin.

17. This scarcely bears out Dr. Gordon's accusation that I am unreasonable, and that I would draw imaginary lines between rodent ulcers and other conditions. Distinguished dermatologists, such as Dr. Percival and Dr. Barber, agree that dermatologists should not treat malignant conditions with radiation.

18. Professor Ahlbom, professor of radio-therapy at the Radium Institute in Stockholm, informed me that the dermatologists of Sweden some years ago wanted to change this position, but were not permitted to do so.

19. The whole position, regarding the use of X-ray apparatus, is chaotic, and I am informed by my Australian colleagues that I am not the only one who has advocated the licensing of X-ray machines. This suggestion has been made in Australia, and in England, where a Government committee is considering the matter at present.

20. When one considers the great precautions taken with radio-active isotopes, the lack of precaution with X-ray machines is fantastic.

21. Even the most highly skilled physician, or radiologist, in America, Britain or South Africa, before obtaining a minute amount of radio-active substance, has to submit an application to a screening committee, which decides whether he is a fit and proper person to use it, or not.

22. Anybody, whether he is trained or not, whether he is a medical man or not, can buy an X-ray machine and proceed to use it.

23. Must the Medical Council of South Africa wait for the licensing of X-ray machines to be introduced in England and America first, before taking action in South Africa? Why not follow the Swedish example and enact that users of X-ray machines must have licences.

24. I am confident that no screening committee would refuse a licence to any dermatologist, or other specialist, who wishes to use an X-ray machine within his recognized sphere, on producing proof that he is qualified to use such a machine.

M. Weinbren

3 Dunkeld Chambers,
Smal Street,
Johannesburg.
3 November 1950.